ANALYSIS OF LIPID PROFILE AMONG KIDNEY TRANSPLANT PATIENTS – A DESCRIPTIVE STUDY

DISSERTATION SUBMITTED FOR

M.D DEGREE (Branch I) GENERAL MEDICINE

MARCH 2007

THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY

CHENNAI, TAMIL NADU.

CERTIFICATE

This is to certify that the dissertation titled ***"ANALYSIS OF LIPID PROFILE AMONG KIDNEY TRANSPLANT PATIENTS – A DESCRIPTIVE STUDY "*** *submitted by* ***Dr. S. RAMESH*** *to the Faculty of General Medicine, The Tamilnadu Dr. M.G.R. Medical university, Chennai in partial fulfillment of the requirement for the award of M.D. Degree (General Medicine) is a bonafide research work carried out by him under our direct supervision and guidance.*

Dr. P. SELVARAJ M.D.,
Professor of Medicine
Chief III Medical Unit,
Department of Medicine,
Madurai Medical College,
Madurai.

Dr. NALINI GANESH M.D.,
Professor and Head
Department of Medicine,
Madurai Medical College,
Madurai.

DECLARATION

I, **Dr. S. RAMESH,** *solemnly declare that the dissertation titled* ***"ANALYSIS OF LIPID PROFILE AMONG KIDNEY TRANSPLANT PATIENTS – A DESCRIPTIVE STUDY"*** *has been prepared by me.*

This is submitted to the ***Tamilnadu Dr. M.G.R. Medical University****, Chennai in partial fulfillment of the rules and regulations for the M.D. Degree Branch I (General Medicine).*

Place : Madurai

Date : *Dr. S. RAMESH*

ACKNOWLEDGEMENT

I express my sincere thanks to former Dean **Dr. Saraswathy M.D.,** and present Dean In Charge **Dr. S. M. Sivakumar M.S.** for permitting me to use the facilities of Madurai Medical College and Govt. Rajaji Hospital to conduct this study.

I will ever remain in gratitude to our Chief **Dr. P. Selvaraj M.D., Prof.** Of Medicine, not only for guiding me throughout the study, but also for being my mentor and source of inspiration during the period of my post graduate training.

Our professor and Head of the Department of Medicine, **Prof. Dr. Nalini Ganesh M.D.**, who has always guided me by valuable words of advice in the conduct of the study and also during my post graduate course. My sincere thanks are due to her.

Knowledge and kindness abounds my beloved teachers **Dr. A. Ayyappan M.D., Dr. M. Kamaraj MD., Dr. Moses K. Daniel MD., Dr. D.D. Venkatraman MD., and Dr. M. Muthiah MD.**, I owe them a lot and my sincere thanks to them.

Our Professor and Head of the Department of Nephrology **Prof. Dr. M. Shanmugaperumal MD., DM., and Dr. V. Velusamy MD.,** Tutor in Nephrology who always guided me by valuable words of advice in the conduct of the study and also during my post graduate course. My sincere thanks are due to them.

I express my heart felt thanks to our Assistant Professors **Dr. M. Natarajan MD., Dr. P. Purushothaman MD., Dr. G. Selvarani MD.,** for their valuable support and guidance through out my study.

My **family and friends** have stood by me during my times of need. Their help and support have been valuable to the study.

I would grossly fail in my duty if I fail to mention here of my **patients** who have ungrudgingly borne the pain and discomfort of investigations. I cannot but pray for their speedy recovery and place this study as a tribute to them and to the numerous others likely affected.

CONTENTS

INTRODUCTION

In advanced stages of kidney failure Transplantation is the treatment of choice. Successful kidney transplant offers the potential for complete rehabilitation. Kidney transplantation is the definitive treatment of ESRD, treating all manifestations of chronic kidney disease. A successful kidney transplant improves the quality of life and reduces the mortality risk for most patients when compared with those on maintenance dialysis. Survival with kidney transplantation is superior to dialysis.

Despite improvement in the short term patient and graft outcomes there has no major improvement in the long term outcome. The incidence of cardiovascular disease (CVD) is very high in patients with chronic kidney (CKD) disease and in kidney transplant recipients. Indeed, available evidence for these patients suggests that the 10-year cumulative risk of coronary heart disease is at least 20%, or roughly equivalent to the risk seen in patients with previous CVD.

Recently, the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (K/DOQI) published guidelines for the diagnosis and treatment of dyslipidemias in patients with CKD, including transplant patients. It was the conclusion of this Work Group that the National Cholesterol Education Program Guidelines are generally applicable to patients with CKD, but that there are significant differences in the approach and

treatment of dyslipidemias in patients with CKD compared with the general population.

Evidence from the general population indicates that treatment of dyslipidemias reduces CVD. Dyslipidemias are very common in CKD and in transplant patients and evidence in kidney transplant patients suggests that judicious treatment can be safe and effective in improving dyslipidemias. However, until recently there have been no adequately powered, randomized, controlled trials examining the effects of dyslipidemia treatment on CVD in patients with CKD.

Cardiovascular disease is the most common cause of post transplant mortality and morbidity among long – term kidney transplant survivors. Patients with post transplantation coronary artery disease tend to be older males, diabetics with higher cholesterol levels, greater incidence of smoking and greater number of acute rejection episodes and as a consequence have received more cumulative doses of steroids. The prevalence of lipid abnormalities after kidney transplantation is very high.

There is need for collaboration among the transplant centre, community nephrologists, and primary care physicians who are involved in the long term care of these patients to enhance the outcome. Prevention and early management of disease progression and addressing the cardiovascular

complications, infections, and malignancies constitute the cornerstone of this collaborative effort to extend the lifespan and allograft function.

Grossly enlarged Cardio vascular disease risk among the transplant patients is due to combination of traditional and non-traditional risk factors. Traditional risk factors include male sex, old age, race, hypertension, diabetes mellitus, sedentary life style, obesity, hyperlipidemia, smoking and postmenopausal state. Hyperuricemia, hyperhomocysteinemia, hyperparathyroidism, proteinuria, systemic inflammation, calcium and phosphorus are the emerging non-traditional risk factors among the kidney transplant patients.

In the recent years there has been much progress made in the understanding the causes and management of the atherosclerotic lipid abnormalities among the kidney transplant patients.

AIMS AND OBJECTIVES

1. To assess the nature of **Lipid profile abnormalities** prevalent among kidney transplant patients.

2. To apply **NKF** recommendations on **Dyslipidemia** management.

3. To critically analyse the data & to interpret its utility for the **Therapeutic interventions**.

REVIEW OF LITERATURE

Chronic kidney disease becomes the global epidemic. Management of such a devastating disease is a highly complicated issue even among the well developed countries.

Medical, ethical, psychological and socio-economic problems associated with chronic kidney disease is a large burden to the healthcare sector of the developing countries like India.

Chronic kidney disease (CKD) is defined as at least 3 months of either:

1. structural or functional abnormalities of the kidney that can lead to kidney failure; or

2. GFR <60 mL/min/1.73m_2.

Causes of Chronic kidney disease includes primary or secondary glomerulonephritis, diabetic nephropathy, hypertensive nephrosclerosis, chronic pyelonephritis, analgesic nephropathy, obstructive uropathy, polycystic kidney disease, vesicoureteric reflux, renal tuberculosis and nephrocalcinosis.

Stages of chronic kidney disease

Stage	Description	GFR (mL/min/1.73m2)
1	**Kidney damage with normal GFR**	**> 90**
2	**Kidney damage with mild reduction of GFR**	**60 – 89**
3	**Moderate reduction of GFR**	**30 – 59**
4	**Severe reduction of GFR**	**15 – 29**
5	**Kidney failure**	**< 15 or dialysis**

ESRD patients at high risk for cardiovascular disease

Age above 65

Diabetes mellitus

MI/Myocardial dysfunction

History of Angina

Long duration ESRD

They should be aggressively screened for **inducible ischemia & myocardial dysfunction (Atleast by stress testing & ECHO)**

Transplantation of the human kidney is frequently the most effective treatment of advanced chronic kidney failure. Worldwide, tens of thousands of such procedures have been performed. When azathioprine and prednisone were initially used as immunosuprressive drugs in the 1960s, the results with properly matched familial donors were superior to those with organs from

cadaveric donors, namely, 75 to 90% compared with 50 to 60% graft survival rates at 1 year. During the 1970s and 1980s, the success rate at the 1-year for cadaveric transplant rose progressively.

By the time cyclosporine was introduced in the early 1980s, cadaveric donor grafts had a 70% 1-year survival and reached the 82% level in the mid-1990s and 88% by 1998. After the first year, graft survival curves show an exponential decline in numbers of functioning grafts from which a half-life (t1/2) in years is calculated; this has increased by 2 years since the 1980s.

Mortality rates after transplantation are highest in the first year and are age-related: 2% for ages 18 to 34 years, 3% for ages 35 to 49 years, and 6.8% for ages over 50 to 60 years. These rates compare favorably to those in the chronic dialysis population, even after risk adjustments for age, diabetes, and cardiovascular status. Most grafts, however, succumb at varying rates to a chronic vascular and interstitial obliterative process termed chronic rejection.

RECIPIENT SELECTION

There are few absolute contraindications to kidney transplantation. The transplant procedure is relatively noninvasive, as the organ is placed in the inguinal fossa without entering the peritoneal cavity. Recipients without perioperative complications can often be discharged from the hospital in excellent condition within 5 days of the operation.

Virtually all end-stage kidney disease (ESRD) patients who receive a transplant have a higher life expectancy than risk-matched patients who remain on dialysis. Even though diabetics or older candidates have a higher mortality rate than other transplant recipients, their survival is improved with transplantation compared to remaining on dialysis. This global benefit of transplantation as a treatment modality poses substantial ethical issues for policy makers, as the number of cadaveric kidneys available is far from sufficient to meet the current needs of the candidates. Waiting lists continue to grow, and the average wait time for a cadaver kidney is now >4 years in many locales. The current standard of care is that the candidate should have a life expectancy of >5 years to be put on a cadaver organ wait list. Even for living donation, the candidate should have >5 years of life expectancy. This is because the benefits of kidney transplantation over dialysis are only realized after a perioperative period in which the mortality is higher in transplanted patients than in dialysis patients with comparable risk profile.

DONOR SELECTION

Types of donor are living related donor, live unrelated donor and cadaveric graft. Living related - offers the advantage of optimally timed surgical procedure, HLA halotype matching, and improved graft survival. Live unrelated donation –option which becomes common place. Consent and HLA halotpye matching is problematic. But comparable graft survival is possible with minimal mismatching.

The living volunteer donors are usually family members selected to have at least partial compatibility for HLA antigens. They should be normal on physical examination and of the same major ABO blood group, because crossing major blood group barriers prejudices survival of the allograft. It is possible, however, to transplant a kidney of a type O donor into an A, B, or AB recipient.

With the acceptance of concept of brain death in India an increasing numbers of cadaveric transplants are being performed. Cadaveric donors should be free of malignant neoplastic disease, hepatitis, and HIV because of possible transmission to the recipient.

Selective renal arteriography should be performed on donors to rule out the presence of multiple or abnormal renal arteries, because the surgical procedure is difficult and the ischemic time of the transplanted kidney is long when vascular abnormalities exist. Transplant surgeons are now using a laparascopic method to isolate and remove the living donor kidney. This operation has the advantage of less evident surgical scars, and, because there is less tissue trauma, the laparoscopic donors have a substantially shorter hospital stay and less discomfort than those who have the traditional surgery. Increased risk of graft failure exists when the donor is elderly or has kidney failure and when the kidney has a prolonged period of ischemia and storage.

Usually Hemodialysis done, before transplantation to ensure a relatively normal metabolic state in recipients. The recipient's own kidneys are left undisturbed. In a transplant operation the donor kidney is placed in a extra peritoneal pouch in the iliac fossa of the recipient. The renal artery and vein are anastomosed to the recipient's iliac vessels. The donor ureter is implanted into the bladder of the recipient.

TISSUE TYPING AND CLINICAL IMMUNOGENETICS

Donor HLA is matched with that of recipient. It is preferable to have a HLA identical donor. If such donor is not available halpo identical (half identical) could be done. Matching for antigens of the HLA major histocompatibility gene complex is an important criterion for selection of donors for kidney allografts. Each mammalian species has a single chromosomal region that encodes the strong, or major, transplantation antigens, and this region on the human sixth chromosome is called HLA.

HLA antigens have been classically defined by serologic techniques, but methods to define specific nucleotide sequences in genomic DNA are increasingly being used.

The Rh system is not expressed on graft tissue. About 5% of HLA-identical kidney allografts are rejected, often within the first weeks after

transplantation. These failures represent states of prior sensitization to non-HLA antigens.

Living Donors

When first-degree relatives are donors, graft survival rates at 1 year are 5 to 7% greater than those for cadaver grafts. The 5-year survival rates still favor the partially matched (3/6 HLA mismatched) family donor over a randomly selected cadaver donor.

For both living and cadaveric donors, the 5-year outcomes are poor if there is a complete (6/6) HLA mismatch. In response to this increasing disparity between cadaver donor supply and patient demand, living unrelated volunteers, usually spouses or close friends, are being accepted as donors in increasing numbers.

The survival rate of living unrelated kidney allografts is as good or better than that of perfectly HLA matched cadaver kidney transplants and comparable to that of kidneys from living relatives. This is likely to be a consequence both of short cold ischemia time and extra care taken to document that kidney function of the donor are optimal before proceeding with a living unrelated donation.

Concern has been expressed regarding the potential risk to a volunteer kidney donor of premature kidney failure after several years of increased blood flow and hyperfiltration per nephron in the remaining kidney. There are

a few reports of the development of hypertension, proteinuria, and even lesions of focal segmental sclerosis in donors under long-term follow-up. Difficulties in donors followed for 20 years are unusual, however, and it may be that having a single kidney becomes significant only when another condition, such as hypertension, is superimposed. It is also desirable to consider the risk of development of type 1 diabetes mellitus in a family member who is a potential donor to a diabetic kidney failure patient.

Anti-insulin and anti-islet antibodies should be measured, and glucose tolerance tests should be performed in such donors to rule out a prediabetic state. It is now possible to remove cadaver kidneys and to maintain them for up to 48 h on cold pulsatile perfusion or simple flushing and cooling. This permits adequate time for typing, cross-matching, transportation, and selection problems to be solved.

HLA Matching and Cadaveric Donors

Now that pooled data on tens of thousands of cadaveric kidney transplants from all over the world are available, the HLA-matching effect can be clearly seen, especially in the long-term survival figures. There is an overall beneficial effect of HLA matching in cadaveric grafts. With increasing numbers of mismatches for cadaveric donors, the 5-year survival drops from 68.2% to 55.3%.

The survival rates at the 10-year mark are projected to range from 65 (zero mismatches) to 34% (six mismatches). Kidneys from HLA-incompatible unrelated or spousal donors do better than those from similarly mismatched cadaver donors, Nevertheless, when such a cadaveric donor is HLA-compatible, the benefit of matching can still be seen.

CARDIOVASCULAR RISKS IN TRANSPLANT PATIENTS:

The leading cause of post transplant death is CVD, responsible for 30%-40% of deaths. Although death rates from CVD are lower than in dialysis patients, they still exceed those of the general population.

Kasiske estimated the cumulative incidence of coronary heart disease, cerebrovascular disease, and peripheral vascular disease at 15 years post transplant to be 23%, 15%, and 15%, respectively. Many risk factors, such as diabetes mellitus, hypertension, hepatitis C virus antibodies (HCV), dyslipidemia, proteinuria, and serum creatinine levels, and hyperhomocysteinemia are overrepresented in Transplant Recipients.

Of course, these risk factors usually arise many years before transplantation, indeed even before dialysis. Thus, reducing the risk of CVD – and indeed, of the other conditions discussed below – requires intervention when patients are either pre-dialysis or on dialysis.

Although the emphasis has traditionally been on the burden of coronary heart disease among kidney transplant patients, recent studies emphasize that the prevalence of cardiomyopathy (presenting clinically as congestive heart failure or as left ventricular enlargement on echocardiography) is significantly increased in these patients.

1year graft survival HLA identical- 95% **1 MISMATCH – 90 TO 95% COMPLETE MISMATCH – 75 TO 80%.** Average half –life of cadaveric grafts is 8yrs. For **HLA** identical living related donor grafts- 20 yrs.

Long-term cadaveric and living donor kidney allograft survival continues to improve. This reflects many factors, including lower rates of **acute rejection** (mainly due to better immunosuppressive regimens), better **antimicrobial prophylaxis**, and probably, improvements in **general medical** and **surgical care**.

Causes of allograft loss after year one

Patient death 50%

Chronic allograft nephropathy 35%

Acute rejection/Non compliance 10%

Recurrent disease 4%

Patient death

No 1 cause is **cardiovascular disease** followed by infection and malignancy.

Measures to improve kidney allograft survival

1. Increase **Living donor** donation – both related & non related.
2. **Preemptive transplantation.**
3. Increase donation from **younger** and previously **healthy cadaveric** donors.
4. **Zero HLA Mismatching**
5. Better donor preparation, improved organ preservation, **faster matching & transplantation**, reduced cold Ischemia time.
6. **ACE inhibitors** and Angiotensin receptor blockers usage.
7. **Nephron dosing** (Matching of donor & recipient age sex, and BMI)
8. **High quality general medical care**. Aggressive control of **Dyslipidemia & Hypertension.**

Effect of HLA-A, -B, -DR Mismatching on Kidney Graft Survival

Degree of Donor mismatch	1-year survival %	5-year survival %
Cadaver donor (all)	89.2	61.3
0/6-HLA mismatch	91.3	68.2
3/6-HLA mismatch	90.1	60.8
6/6-HLA mismatch	85.2	55.3
Living related donor (all)	94.7	76.0
0/6-HLA mismatch	96.7	87.0
3/6-HLA mismatch	94.3	73.2
6/6-HLA mismatch	92.7	57.7
Living unrelated donor	95.3	77.4

Presensitization

A positive cross match of recipient serum with donor T lymphocytes representing anti-HLA class I is usually predictive of an acute vasculitic event termed hyperacute rejection. Patients with anti-HLA antibodies can be safely transplanted if careful cross-matching of donor blood lymphocytes with recipient serum is performed. Patients sustained by dialysis often show fluctuating antibody titers and specificity patterns. At the time of assignment of a cadaveric kidney, cross matches are performed with at least a current serum.

Techniques for cross-matching are not universally standardized; however, at least two techniques are employed in most laboratories. The minimal purpose for the cross match is avoidance of hyperacute rejection mediated by recipient antibodies to donor HLA class I antigens. Sensitive tests, such as the use of flow cytometry, can be useful for avoidance of accelerated, and often untreatable, early graft rejection in patients receiving second or third transplants.

Donor T lymphocytes, which express only class I antigens, are used as targets for detection of anti-class I (HLA-A and -B) antibodies. Preformed anti-class II (HLA-DR) antibodies against the donor carry a higher risk of graft loss as well, particularly in recipients who have suffered early loss of a prior kidney transplant. B lymphocytes expressing both class I and class II antigens are used in these assays.

Drugs for Immunosuppression

Azathioprine, an analogue of mercaptopurine, was for two decades the keystone to immunosuppressive therapy in humans. This agent can inhibit synthesis of DNA, RNA, or both. Because cell division and proliferation are a necessary part of the immune response to antigenic stimulation, suppression by this agent may be mediated by the inhibition of mitosis of immunologically competent lymphoid cells, interfering with synthesis of DNA. Alternatively, immunosuppression may be brought about by blocking

the synthesis of RNA (possibly messenger RNA), inhibiting processing of antigens prior to lymphocyte stimulation. Therapy with azathioprine in doses of 1.5 to 2.0 mg/kg per day is generally added to cyclosporine as a means of decreasing the requirements for the latter. Because azathioprine is rapidly metabolized by the liver, its dosage need not be varied directly in relation to kidney function, even though kidney failure results in retention of the metabolites of azathioprine. Reduction in dosage is required because of leukopenia and occasionally thrombocytopenia. Excessive amounts of azathioprine may also cause jaundice, anaemia, and alopecia.

Mycophenolate mofetil is now used in place of azathioprine in many centers. It has a similar mode of action and a mild degree of gastrointestinal toxicity but produces minimal bone marrow suppression. Its advantage is its increased potency in preventing or reversing rejection.

Glucocorticoids are important adjuncts to immunosuppressive therapy. Prednisone has effects that are easiest to assess, and in large doses it is usually effective for the reversal of rejection. In general, 200 to 300 mg prednisone is given immediately prior to or at the time of transplantation, and the dosage is reduced to 30 mg within a week. The side effects particularly impairment of wound healing and predisposition to infection, make it desirable to taper the dose as rapidly as possible.

A major effect of steroids is on the monocyte-macrophage system, preventing the release of interleukin (IL) 6 and IL-1. Lymphopenia after large doses of glucocorticoids is primarily due to sequestration of recirculating blood lymphocytes to lymphoid tissue.

Cyclosporine is a fungal peptide with potent immunosuppressive activity. It is a cyclic 11- amino peptide derived from the fungus. It has a narrow therapeutic window. It acts on the calcineurin pathway to block transcription of mRNA for IL3-2 and other proinflammatory cytokines, thereby inhibiting T cell proliferation. Since it blocks production of IL-2 by T cells, its combination with steroids is expected to produce a double block in the macrophage-IL-6/IL-1- T cell- IL-2 sequence. Of its toxic effects (nephrotoxicity, hepatotoxicity, hirsutism, tremor, gingival hyperplasia, diabetes), only **nephrotoxicity** presents a serious management problem.

The increased cardiovascular risk profile as a result of cyclosporine is ascribed to both a quantitative increase in LDL particles and an increased oxidizability of the LDL particles. Use of it is also associated with increased plasma lipoprotein(a) (Lp[a]) and homocysteine levels, In addition, It has unfavorable effects on the fibrinolytic system also. Cyclosporine leads to an elevation of BP. These side effects contributes to the high cardiovascular morbidity & to an accelerated loss of graft function.

Tacrolimus (FK-506) is a fungal macrolide that has the same mode of action, and a similar side effect profile, as cyclosporine. It does not produce hirsutism or gingival hyperplasia, however. De novo induction of diabetes mellitus is more common with tacrolimus.

Conversion from **cyclosporine to tacrolimus** reduced not only the serum concentration of LDL cholesterol but also the **oxidizability of the LDL** particle. The reduced oxidizability of the LDL particles is likely to be associated with the concurrent decrease in serum triglycerides. Reduced levels of serum triglycerides and apolipoprotein B are associated with an altered, less dense composition of the LDL particles. These lighter LDL particles contain more lipids compared with the protein component, resulting in conformational changes with a diminished access for free radicals and pro-oxidants such as copper to cause oxidation of the fatty acids. Furthermore, lighter LDL particles are more easily cleared from the circulation by the high-affinity LDL receptor, leading to a shorter plasma residence time, during which the particle is susceptible to *in vivo* oxidation.

Sirolimus (previously called rapamycin) is another fungal macrolide but has a different mode of action, i.e., it inhibits T cell growth factor pathways, preventing the response to IL3-2 and other cytokines. It can be used in conjunction with cyclosporine or tacrolimus as an alternative immunosuppressive regimen.

Antibodies to Lymphocytes When serum from animals made immune to host lymphocytes is injected into the recipient, a marked suppression of cellular immunity to the tissue graft results. A globulin fraction of serum **[antilymphocyte globulin (ALG)]** is the agent generally employed. For use in humans, peripheral human lymphocytes, thymocytes, or lymphocytes from spleens or thoracic duct fistulas have been injected into horses, rabbits, or goats to produce antilymphocyte serum, from which the globulin fraction is then separated.

Monoclonal antibodies against defined lymphocyte subsets offer a more precise and standardized form of therapy. OKT3 is directed to the CD3 molecules that form a portion of the T cell antigen-receptor complex; hence CD3 is expressed on all mature T cells. CD4 or CD8 molecules also form part of the fully activated cluster of molecules, and monoclonal antibodies to these offer the potential for more selective targeting of T cell subsets.

Another approach to more selective therapy is to target the 55-kDa alpha chain of the IL3-2 receptor, expressed only on T cells that have been recently activated. The problem with such mouse antibodies is the potential for developing human antimouse antibodies (HAMA).

Genetically engineered monoclonal antibodies can solve this problem. Two such antibodies to the IL-2 receptor, in which either a chimeric protein has been made between mouse Fab with human Fc (basiliximab) or

"humanized" by splicing the combining sites of the mouse into a molecule that is 90% human IgG (daclizumab), have been approved for prophylaxis of acute rejection in the immediate posttransplant period. They are effective at decreasing the acute rejection rate and have few adverse side effects.

LIPOPROTEIN METABOLISM

Lipoproteins are large, mostly spherical complexes that transport lipids (primarily triglycerides, cholesteryl esters), and fat-soluble vitamins through body fluids (plasma, interstitial fluid, and lymph) to and from tissues. They play an essential role in the absorption of dietary cholesterol, long-chain fatty acids, and fat-soluble vitamins; the transport of triglycerides, cholesterol, and fat-soluble vitamins from the liver to peripheral tissues; and the transport of cholesterol from peripheral tissues to the liver.

Lipoproteins contain a core of hydrophobic lipids (triglycerides and cholesteryl esters) surrounded by hydrophilic lipids (phospholipids, unesterified cholesterol) and proteins that interact with body fluids. The plasma lipoproteins are divided into five major classes based on their relative densities): chylomicrons, very low density lipoproteins (VLDL), intermediate-density lipoproteins (IDL), low-density lipoproteins (LDL), and high-density lipoproteins (HDL).

Each lipoprotein class comprises a family of particles that vary slightly in density, size, migration during electrophoresis, and protein composition.

The density of a lipoprotein is determined by the amount of lipid and protein per particle. HDL is the smallest and most dense lipoprotein, whereas chylomicrons and VLDL are the largest and least dense lipoprotein particles. Most triglyceride is transported in chylomicrons or VLDL, and most cholesterol is carried as cholesteryl esters in LDL and HDL.

The apolipoproteins are required for the assembly and structure of lipoproteins. Apolipoproteins also serve to activate enzymes important in lipoprotein metabolism and to mediate the binding of lipoproteins to cell-surface receptors. ApoA-I, which is synthesized in the liver and intestine, is found on virtually all HDL1 particles. ApoA-II is the second most abundant HDL apolipoprotein and is found on approximately two-thirds of all HDL particles.

ApoB is the major structural protein of chylomicrons, VLDL, IDL, and LDL. One molecule of apoB, either apoB-48 (chylomicrons) or apoB-100 (VLDL, IDL, or LDL), is present on each lipoprotein particle. The human liver makes only apoB-100, and the intestine makes apoB-48. ApoE is present in multiple copies on chylomicrons, VLDL, and IDL and plays a critical role in the metabolism and clearance of triglyceride-rich particles. Three apolipoproteins of the C-series (apoC-I, -II, and -III) also participate in the metabolism of triglyceride-rich lipoproteins.

TRANSPORT OF DIETARY LIPIDS (EXOGENOUS PATHWAY)

Dietary triglycerides are hydrolyzed by pancreatic lipases within the intestinal lumen and are emulsified with bile acids to form micelles. Dietary cholesterol and retinol are esterified (by the addition of a fatty acid) in the enterocyte to form cholesteryl esters and retinyl esters, respectively.

Longer-chain fatty acids (>12 carbons) are incorporated into triglycerides and packaged with apoB-48, cholesteryl esters, retinyl esters, phospholipids, and cholesterol to form chylomicrons. Nascent chylomicrons are secreted into the intestinal lymph and delivered directly to the systemic circulation, where they are extensively processed by peripheral tissues before reaching the liver. The particles encounter lipoprotein lipase (LPL), which is anchored to proteoglycans that decorate the capillary endothelial surfaces of adipose tissue, heart, and skeletal muscle. The triglycerides of chylomicrons are hydrolyzed by LPL, and free fatty acids are released; apoC-II, which is transferred to circulating chylomicrons, acts as a cofactor for LPL in this reaction. The released free fatty acids are taken up by adjacent myocytes or adipocytes and either oxidized or reesterified and stored as triglyceride. Some free fatty acids bind albumin and are transported to other tissues, especially the liver.

The chylomicron particle progressively shrinks in size as the hydrophobic core is hydrolyzed and the hydrophilic lipids (cholesterol and

phospholipids) on the particle surface are transferred to HDL. The resultant smaller, more cholesterol ester-rich particles are referred to as chylomicron remnants. The remnant particles are rapidly removed from the circulation by the liver in a process that requires apoE.

TRANSPORT OF HEPATIC LIPIDS (ENDOGENOUS PATHWAY)

This one refers to the hepatic secretion and metabolism of VLDL to IDL and LDL. VLDL particles resemble chylomicrons in protein composition but contain apoB-100 rather than apoB-48 and have a higher ratio of cholesterol to triglyceride (~1 mg of cholesterol for every 5 mg of triglyceride). The triglycerides of VLDL are derived predominantly from the esterification of long-chain fatty acids.

The packaging of hepatic triglycerides with the other major components of the nascent VLDL particle (apoB-100, cholesteryl esters, phospholipids, and vitamin E) requires the action of the enzyme microsomal transfer protein (MTP). After secretion into the plasma, VLDL acquires multiple copies of apoE and apolipoproteins of the C series. The triglycerides of VLDL are hydrolyzed by LPL, especially in muscle and adipose tissue.

As VLDL remnants undergo further hydrolysis, they continue to shrink in size and become IDL, which contain similar amounts of cholesterol and triglyceride. The liver removes approximately 40 to 60% of VLDL remnants and IDL by LDL receptor-mediated endocytosis via binding to apoE. The

remainder of IDL is remodeled by hepatic lipase (HL) to form LDL; during this process, most of the triglyceride in the particle is hydrolyzed and all apolipoproteins except apoB-100 are transferred to other lipoproteins.

The cholesterol in LDL accounts for ~70% of the plasma cholesterol in most individuals. Approximately 70% of circulating LDLs are cleared by LDL receptor-mediated endocytosis in the liver. Lipoprotein(a) [Lp(a)] is a lipoprotein similar to LDL in lipid and protein composition, but it contains an additional protein called apolipoprotein(a) [apo(a)]. Apo(a) is synthesized in the liver and is attached to apoB-100 by a disulfide linkage. The mechanism by which Lp(a) is removed from the circulation is not known.

HDL METABOLISM AND REVERSE CHOLESTEROL TRANSPORT

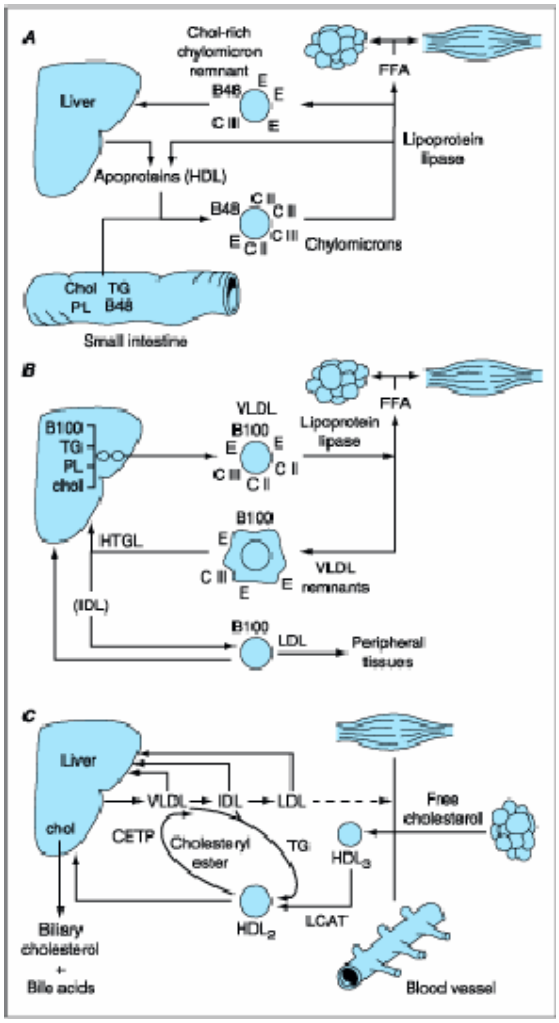
All nucleated cells synthesize cholesterol but only hepatocytes can efficiently metabolize and excrete cholesterol from the body. The predominant route of cholesterol elimination is by excretion into the bile, either directly or after conversion to bile acids. Cholesterol in peripheral cells is transported from the plasma membranes of peripheral cells to the liver by an HDL-mediated process termed **reverse cholesterol transport.**

Nascent HDL particles are synthesized by the intestine and the liver. The newly formed discoidal HDL particles contain apoA-I and phospholipids (mainly lecithin) but rapidly acquire unesterified cholesterol and additional phospholipids from peripheral tissues via transport by the membrane protein

ATP-binding cassette protein A (ABCA). Once incorporated in the HDL particle, cholesterol is esterified by lecithin-cholesterol acyltransferase (LCAT), a plasma enzyme associated with HDL. As HDL acquires more cholesteryl ester it becomes spherical, and additional apolipoproteins and lipids are transferred to the particles from the surfaces of chylomicrons and VLDL during lipolysis.

HDL cholesterol is transported to hepatoctyes by both an indirect and a direct pathway. HDL cholesteryl esters are transferred to apoB-containing lipoproteins in exchange for triglyceride by the cholesteryl ester transfer protein (CETP). The cholesteryl esters are then removed from the circulation by LDL receptor-mediated endocytosis. HDL cholesterol can also be taken up directly by hepatocytes via the scavenger receptor class BI (SR-BI), a cell-surface receptor that mediates the selective transfer of lipids to cells.

HDL particles undergo extensive remodeling within the plasma compartment as they transfer lipids and proteins to lipoproteins and cells. For example, after CETP-mediated lipid exchange, the triglyceride-enriched HDL becomes a subbstrate for HL, which hydrolyzed the triglycerides and phospholipids to generate smaller HDL particles.



Transport of endogenous hepatic lipids via VLDL, IDL, and LDL. Note the relative and absolute changes in apoproteins, other than apo B100, as VLDL is converted to IDL and LDL. The sites of action of the two lipases, LPL and HTGL, are denoted.

Transport of exogenously derived lipids from the intestine to peripheral tissues and liver via the chylomicron system.

HDL metabolism and the role of HDL in reverse cholesterol transport. Free cholesterol is accepted from peripheral tissues by HDL_3 and, after esterification, may be transferred to apo B100 lipoproteins.

Table 344-2. Physical-Chemical Characteristics of the Major Lipoprotein Classes

Lipoprotein	Density, g/dL	Molecular Mass, kDa	Diameter, nm	Lipid, %[a]		
				TG	Chol	PL
Chylomicrons	0.95	400×10^3	75-1200	80-95	2-7	3-9
VLDL	0.95-1.006	$10\text{-}80 \times 10^3$	30-80	55-80	5-15	10-20
IDL	1.006-1.019	$5\text{-}10 \times 10^3$	25-35	20-50	20-40	15-25
LDL	1.019-1.063	2.3×10^3	18-25	5-15	40-50	20-25
HDL	1.063-1.210	$1.7\text{-}3.6 \times 10^2$	5-12	5-10	15-25	20-30

[a] The remaining percent composition is made up of the apoproteins.

NOTE: TG, triglyceride; Chol, the sum of free and esterified cholesterol; PL, phospholipid; VLDL, very low density lipoprotein; IDL, intermediate density lipoprotein; LDL, low-density lipoprotein; HDL, high-density lipoprotein.

Dyslipidemia in kidney Transplants:-

Dyslipidemia, alone or as part of the metabolic syndrome, is an established risk factor for CVD mortality in kidney transplant recipients , The main causes are thought to be steroids, calcineurin inhibitors, sirolimus, Diuretics and Betablockers.

About 60% of kidney transplant recipients have a total cholesterol level greater than 240 mg/dL (6.21 mmol/L); and low-density lipoprotein cholesterol (LDL-C) greater than 130 mg/dL (3.36 mmol/L); about 35% have hypertriglyceridemia. Low levels of high-density lipoprotein cholesterol (<35 mg/dL [0.91 mmol/L]) occur in about 15% of kidney transplant recipients-a percentage similar to that in the general population. The concentrations of lipoprotein(a) and small, dense LDL-C, which are atherogenic, is increased.

Oxidatively modified LDL cholesterol is a chemotactic factor for monocytes and macrophages, both in vascular endothelium and in kidney glomeruli, and it may cause activation of endothelial cells, smooth muscle cells, mesangial cells, and macrophages. Studies showed deposition of LDL and oxidized LDL in a mesangiocapillary way in the glomeruli, in endothelial cells, and in the interstitial space. The amount of oxidized LDL immunostaining was related to the increase in the density of macrophages in the tubulointerstitial compartment and to the extent of interstitial fibrosis.

Cyclosporine increases serum LDL cholesterol level by inhibiting the synthesis of LDL receptors in the liver, thereby interfering with the LDL receptor–mediated catabolism in the liver. The improvement in serum LDL cholesterol level after conversion to tacrolimus might be due to the withdrawal of this inhibition of the LDL receptor production. The atherogenicity of LDL cholesterol depends not only on its serum concentration but also on the oxidizability of the particles.

Interestingly, the vascular lesions of chronic allograft nephropathy seen on allograft biopsy resemble those of atherosclerosis. Because of the high prevalence of CVD in transplant recipients, it is reasonable to consider the kidney transplant state to be **“coronary heart disease risk equivalent”** when applying the guidelines.

Immunosuppressants in Kidney transplants:

CYCLOSPORINE

Lipid profile abnormalities starts within one month of initiation of therapy. Typically it includes increases upto 30% in total cholesterol, 21 to 69%in triglyceride, 5 to 57%in LDL, 0 to 61% HDL, It also produces an increased oxidizadility of LDL particles & increased plasma lipoprotein LP and homocysteine level. It produces unfavourable effect on fibrinolytic system also.

Tacrolimus usage is associated with less unfavourable effects on hypertension and lipid profile. With conversion to tacrolimus reduction in LDL level and the LDL particles are less susceptible to oxidation.

Antiproliferative agents. Sirolimus has been shown to increase apo B -100, apo C –II, apo C – III,and hepatic VLDL cholesterol production and to decrease heparin induced LPL activity. Often results in increased total cholesterol and triglyceride. This effect appears to be greater than with cyclosporine or tacrolimus.

Corticosteroids It enhance activity of acetyl–coenzyme A carboxylase, 3–hydroxy 3- methyl glutaryl-coenzyme A and free fatty acid synthase and inhibit LPL activity. So steroids enhance cholesterol production and prevent the breakdown of TG rich particles. Combination of steroids with immunosuppressive agents have additive effects due to different mechanisms of lipid profile alteration.

Anti Hypertensive drugs in Kidney Transplants:

1) Beta blockers

They increase **TG & reduce HDL.** Those with Beta 1 selectivity & partial agonistic activity have less effect on lipid profile. Non selective Beta blockers reduce HDL up to 20% and raise TG up to 50%. VLDL/TG metabolism retarded in the setting of unopposed alpha adrenergic stimulation of lipoprotein lipase activity. So low VLDL metabolism results in reduction of HDL.

ii) Loop Diuretic & Thiazides

They increase the plasma concentration of **TC,TG, LDL & Decrease HDL** average 5 to 20% during initiation of treatment. It may be related to ECV depletion and Nacl restriction. Also hypokalemia mediated reduced insulin secretion may be contributory factor. Serum cholesterol returns to baseline over 3 to 12 months of therapy.

iii) Calcium Channel Blockers

In the usual therapeutic doses they have no effect on serum glucose, insulin secretion and insulin sensitivity. They **do not increase TG and Cholesterol**. No reduction of HDL seen. Ideal for diabetic and patients of dysmetabolic syndrome.

iv) Central Alpha2 Adrenergic Agonists

They are **neutral** with respect to Lipid metabolism.

Dyslipidemias as defined in the Adult Treatment Panel III Guidelines

Dyslipidemia	Level (mg/dL)
Total cholesterol	
Desirable	<200
Borderline high	200–239
High	>240
LDL cholesterol	
Optimal	<100
Near optimal	100–129
Borderline	130–159
High	160–189
Very high	>190
Triglycerides	
Normal	<150
Borderline high	150–199
High	200–499
Very high	>500
HDL cholesterol	
Low	<40

Factors associated with post-transplant dyslipidemia

TRADITIONAL RISK FACTORS

1. Male gender
2. Genetic predisposition
3. Increased age
4. Proteinuria

5. Kidney dysfunction

6. Medications

★ **Immunosuppressive agents**

- Calcineurin inhibitors (cyclosporine, tacrolimus)
- Antiproliferative agents (sirolimus)
- Corticosteroids

★ **Antihypertensive agents**

- Diuretics
- Beta-blockers

NONTRADITIONAL RISK FACTORS

1. Homocysteine
2. Oxidative stress
3. Proteinuria
4. Inflammation
5. C-reactive protein
6. Left ventricular hypertrophy
7. Hyperparathyroidism
8. Thrombogenic factors.

Mechanisms of Iatrogenic dyslipidemia in kidney transplant recipients

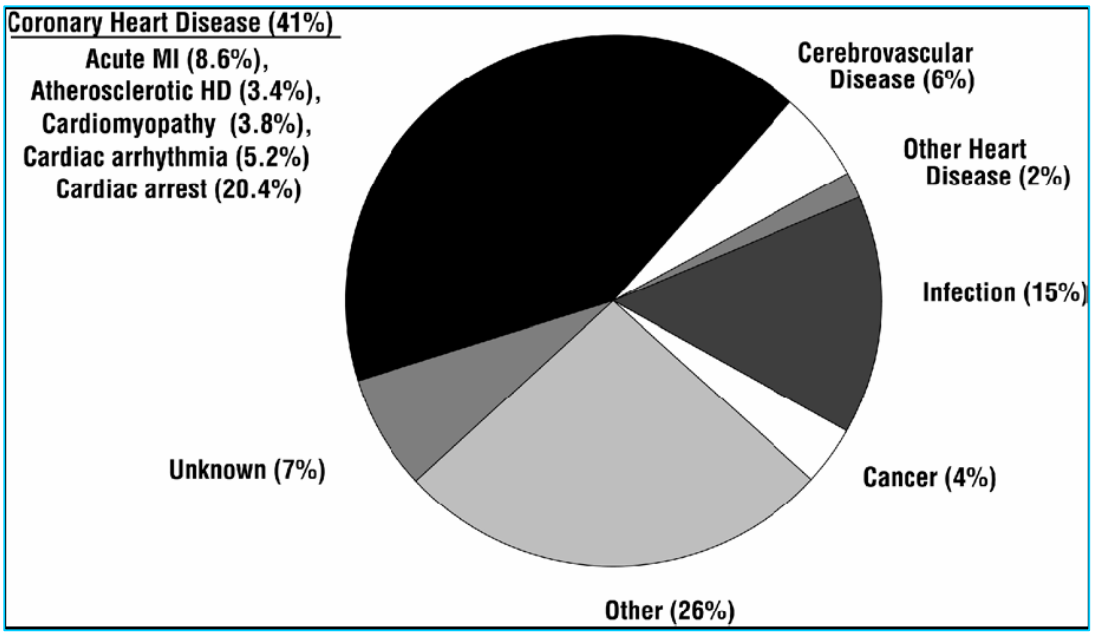
1. Reduction of bile acid synthesis
2. Altered hepatic LDL receptor activity

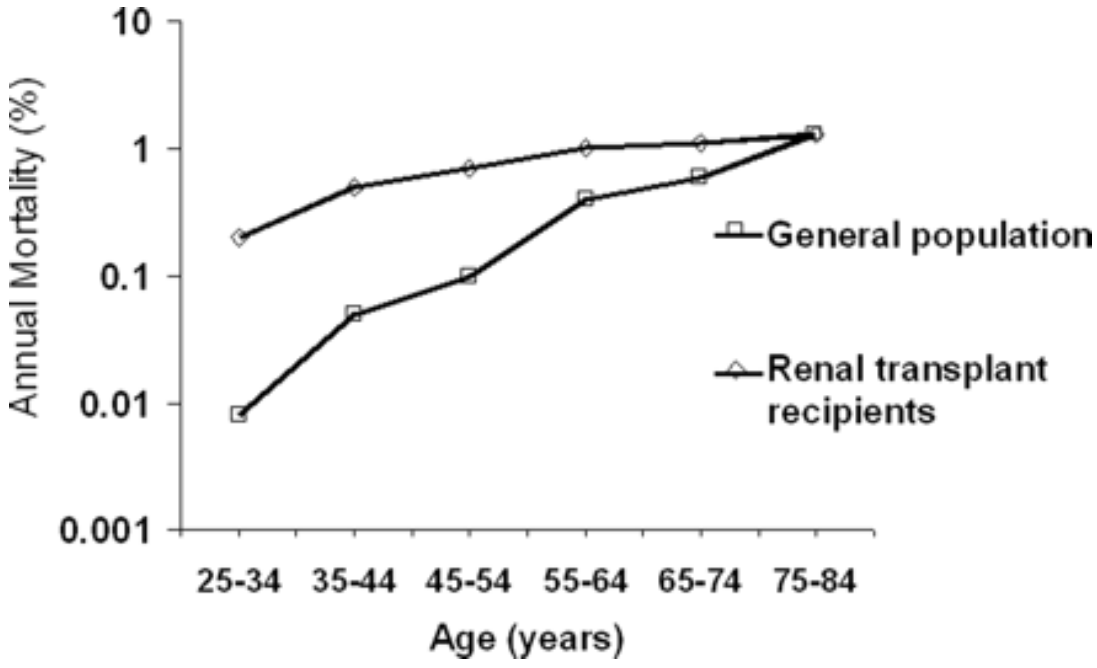
3. Increased hepatic triglyceride lipase activity
4. Inhibition of lipoprotein lipase.
5. Increased lecithin-cholesterol acyltransferases.
6. Increased LDL oxidation
7. Enhanced HMG-CoA activity
8. Enhanced acety1-coenzyme A carboxylase.
9. Increased free fatty acid synthetase

Key features of the NKF-K/DOQI Guidelines that differ from those of the National Cholesterol Education Program Adult Treatment Panel II NKF-K/DOQI Guidelines

1. CKD and kidney transplant patients should be considered to be in the highest risk category and evaluation of **dyslipidemias** should occur at presentation after a change in status, and annually as well.
2. Drug therapy should be used for **LDL 100–129 mg/dL** after 3 months of **TLC.**
3. Initial drug therapy for high LDL should be with a **statin**.
4. Fibrates may be used in Stage 5 CKD
    a) For patients with triglycerides >500 mg/dL; and
    b) For patients with triglycerides >200 mg/dL with non-HDL Cholesterol >130 mg/dL, who do not tolerate statins.
5. Gemfibrozil may be the fibrate of choice for treatment of high triglycerides in patients with CKD and kidney transplant patients

Causes of death among patients, treated with hemodialysis, peritoneal dialysis, or kidney transplantation





THE MANAGEMENT OF DYSLIPIDEMIAS IN ADULT KIDNEY TRANSPLANT RECIPIENTS

Dyslipidemia (mg/dL)	Goal (mg/dL)	Initiate	Increase
TG >500	<500	TLC	Fibrate or Niacin
LDL 100–129	<100	TLC	Low dose statin
LDL >130	<100	Low dose statin	Max. dose statin
TG >200 and Non-HDL >130	Non-HDL <130	TLC+ Low dose statin	Max. dose statin

THERAPEUTIC LIFESTYLE CHANGES (TLC) FOR ADULT KIDNEY TRANSPLANT RECIPIENTS

Diet (consult a dietitian with expertise in chronic kidney disease)

1. Emphasize **reduced saturated fat**
2. Saturated fat: <7% of total calories
3. Polyunsaturated fat: up to 10% of total calories
4. Monounsaturated fat: up to 20% of total calories
5. Total fat: 25–35% of total calories
6. **Cholesterol:** <200 mg per day
7. Carbohydrate: 50–60% of total calories
8. Emphasize components that reduce dyslipidemia
9. Fiber: 20–30 g per day, emphasize 5–10 g per day viscous (soluble) fiber.

10. Consider plant stanols/sterols 2 g per day

11. **Improve glycemic control**

12. Emphasize total calories to attain/maintain standard

    NHANES body weight

13. Match intake of overall energy (calories) to overall energy needs.

14. **Body mass index 25–28 kg/m2**

15. Waist circumference

    Men <40 inches (102 cm)

    Women <35 inches (88 cm)

16. **Waist–hip ratio (men <1.0; women <0.8)**

Physical activity

1. **Moderate daily lifestyle activities**

2. Use pedometer to attain/maintain 10,000 steps per day

3. **Emphasize regular daily motion and distance (within ability)**

4. Moderate planned physical activity

    - 3–4 times per week 20–30 minute periods of activity
    - Include 5-minute warm-up and cool-down
    - Choose walking, swimming, supervised exercise (within ability)
    - Include resistance exercise training

5. **Emphasize lean muscle mass and reducing excess body fat**

Habits

★ **Alcohol in moderation:** limit one drink per day with approval of physician.

★ **Smoking cessation.**

Exercise training produces small, but significant improvements in dyslipidemias. It has a number of beneficial effects, independent of those on dyslipidemias, and the lack of adverse effects makes a compelling case for recommending exercise in patients at risk for ACVD. The reduction in LDL that can be achieved with TLC is generally modest. Therefore, TLC alone is usually insufficient to reduce the LDL to the goal of <100mg/dL (<2.59mmol/L). In patients who cannot reduce LDL to <100mg/dL (<2.59mmol/L) by diet, a statin should be prescribed, Diet should be continued as an adjunct to the statin. Strategy to find out the lowest effective dose that achieves the goal, will minimize the frequency and severity of adverse effects.

The 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors **("statins")** are currently the most effective agents for lowering LDL-C levels. Statins are coadministered with other substrates of CYP3A4 enzymes. Generally, in patients who are also taking a **calcineurin inhibitor**, the statin dose should be reduced to about **half the standard dose.**

To minimise statin toxicity, start with low dose statin. Use of pravastatin or Fluvastatin had associated with least interaction with Cycloporine. Periodic checking of plasma CK and Liver function tests recommended.

The reduction in mortality and in CHD events is proportional to the reduction in LDL. Statins are safe and effective in reducing LDL in kidney transplant recipients. Furthermore, statins reduce **the incidence of cardiac death and acute myocardial infarction** in these patients, Elevated hepatic transaminases occur in 0.5–2.0% of patients treated with statins in the general population. Therefore, baseline **alanine and aspartate transferase levels** should be obtained. Statins have not been shown to worsen outcomes in patients with chronic transaminase elevations due to hepatitis B or C.

Patients should also be monitored for signs and symptoms of **myopathy**. The risk of myopathy from statins is increased by CKD, advanced age, small body frame, and concomitant medications (e.g. fibrates, nicotinic acid, cyclosporine, azole antifungals, macrolide antibiotics, protease inhibitors, nondihydropyridine calcium antagonists, and amiodarone). Obtaining a baseline **creatinine phosphokinase (CK)** level will help in the interpretation of subsequent CK levels.

Patients who develop muscle pain or tenderness should discontinue statin therapy immediately and have CK levels measured. Elevations greater than 10 times the upper limit of normal are indicative of myositis and require atleast temporary cessation of statin therapy. For patients with muscle soreness and either normal or mildly elevated CK, levels should be measured weekly, and the patient’s symptoms monitored closely. Frequently, symptoms may improve with a reduction in the dose of the statin. However, if symptoms worsen, the statin should be discontinued.

Recommended daily statin dose ranges

Statin	Level of GFR (mL/min/1.73 m2)		
	≥30	≤30 or dialysis	With cyclosporine
Atorvastatin	10–80 mg	10–80 mg	10–40 mg
Fluvastatin	20–80 mg	10–40 mg	10–40 mg
Lovastatin	20–80 mg	10–40 mg	10–40 mg
Pravastatin	20–40 mg	20–40 mg	20–40 mg
Simvastatin	20–80 mg	10–40 mg	10–40 mg

Maximum doses of fibrates in patients with reduced kidney function

Fibrate	Dose (mg) by level of GFR (mL/min/1.73 m2)			
	>90	60–90	15–59	<15
Bezafibrate	200 tid	200 bid	200 qd	Avoid
Clofibrate	1,000 bid	1,000 qd	500 qd	Avoid
Fenofibrate	201 qd	134 qd	67 qd	Avoid
Gemfibrozil	600 bid	600 bid	600 bid	600 bid

Chronic allograft nephropathy (CAN) is the main cause of late graft loss in kidney transplantation. The pathogenesis of CAN is multifactorial. The initiating factors are probably mainly immunologic, whereas the perpetuating

factors are considered to be largely nonimmunologic, including **hyperlipidemia and hypertension.**

The most significant factors associated with CV events were as follows: gender, length of smoking, diabetes mellitus. Of note, even a nonfatal posttransplantation myocardial infarction may predict future graft failure and death. Peripheral vascular disease (cerebral vascular disease and lower extremity vascular disease) afflicts at least 15% of all kidney transplant recipients in a 10- to 15-yr period posttransplantation.

In recognition that lipid alterations in these patients are linked with development of ischemic heart disease, vascular mortality, and graft deterioration, the **National Kidney Foundation** has recently released guidelines suggesting a low-density-lipoprotein **(LDL) cholesterol goal of < 100 mg/dL** for these patients. **Statins and diet therapy** are recommended as first-line agents for achieving goal LDL cholesterol levels in this population.

All statins can provide a 30 to 40% reduction in LDL cholesterol levels. Patients who require maximal LDL cholesterol lowering may be treated with atorvastatin or simvastatin, whereas patients with low HDL cholesterol may have a greater advantage from simvastatin use and those with elevated triglycerides may benefit from high-dose atorvastatin. The final choice of statins should be left to the judgment of the treating physician. For the treatment of hypertriglyceridemia, particularly in patients who are treated

with sirolimus, gemfibrozil may be the fibric derivative of choice. Although nicotinic acid derivatives also could be used, fibric acid derivatives are better tolerated. Bile acid sequestrants such as cholestyramine, colestipol, and colesevelam hydrochloride alter the bioavailability of immunosuppressants and also may increase triglyceride levels. Ezetimibe was used recently alone and in combination with statins to reduce LDL cholesterol in a small-size study with kidney transplant patients. Antilipemic drugs may have significant interactions between the classes and with immunosuppressant agents. Statins and fibrates interact with CNI and may result in hepatitis, myositis, and rhabdomyolysis. The prevalence of these untoward effects is minimal in our contemporary era of immunosuppression in the absence of high-dose fibrate or statin therapy and with close monitoring.

In summary, adult kidney transplant recipients with hypertriglyceridemia (triglycerides 300 mg/dl, or 5.65 mmol/L) may be treated with fibrates, and statins can be used for LDL cholesterol levels of 100 mg/dl (2.59 mmol/L;). Treatment of proteinuria and other causes of secondary dyslipidemia, along with therapeutic lifestyle changes including diet and physical activity, always should be combined.

The National Kidney Foundation Task Force on Cardiovascular Disease recommends that kidney transplant recipients are considered as being in the **highest risk category** when these guidelines are applied. Therefore, the goal for the **LDL-C value** for kidney transplant recipients should generally be **100 mg/dL (2.59 mmol/L).**

MATERIALS AND METHODS

MATERIALS AND METHODS

Setting : kidney transplant patients attending transplant op, of Nephrology Department and healthy volunteers attending Medicine OPD.

Collaborating Departments **:** Department of Nephrology
Madurai Medical College
Madurai.
Department of Biochemistry
Madurai Medical College
Madurai

Design of the study **:** Descriptive study

Period of study **:** 1.8.2005 to 31.5.2006

Sample size **:** 40

Selection of the study subjects

40 kidney transplant patients attending Transplant OPD, Department of Nephrology,Govt. Rajaji Hospital between 1.8.2005 to 31.5.2006 formed the study group.

DEFINITIONS

Chronic kidney disease (CKD) At least 3 months of either: 1) structural or functional abnormalities of the kidney that can lead to kidney failure; or 2) GFR <60 mL/min/1.73m2

Cardiovascular Disease (CVD) Coronary heart disease, cerebrovascular disease, renal artery stenosis, peripheral vascular disease, congestive heart failure, or left ventricular hypertrophy

Atherosclerotic cardiovascular disease (ACVD) Coronary heart disease, cerebrovascular disease, renal artery stenosis, or peripheral vascular disease

Coronary heart disease (CHD) Atherosclerotic disease of the coronary arteries that causes myocardial ischemia

Cerebrovascular disease Atherosclerotic disease of the cerebral arteries that causes strokes and transient ischemic attacks

Peripheral vascular disease Atherosclerotic disease of arteries that causes ischemia of the extremities

Dyslipidemia Any abnormality in plasma lipoprotein concentration or composition that is associated with an increased risk for atherosclerotic cardiovascular disease

Lipid profile Plasma levels of total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol and triglycerides

GFR glomerular filtration rate.

Inclusion criteria

40 kidney transplant patients attending Transplant OPD, Nephrology department.

Exclusion criteria

1. Kidney failure
2. Clinical and or laboratory evidence of graft rejection
3. Acute or chronic infections
4. Diabetes,
5. Hypothyroidism,
6. Liver disease,
7. Excessive alcohol consumption and smoking.
8. Nephrotic syndrome

Methods

History

1. Diabetes mellitus
2. Family history of premature **CAD**
3. Dietary habits,
4. Probable cause of kidney failure
5. Time lag prior to transplant
6. Mode of renal replacement therapy offered prior to transplant
7. Nature of donor & compatibility
8. Drug regimen

9. Amount of weight gain

10. Intercurrent infections

11. Any rejection episodes & hospitalization in the recent past

12. Other comorbid medical illness

Clinical Examination

1. Height, weight, **Body mass index**

2. Vital parameters

3. Major systems examination

4. Evidence of active infections / graft rejection.

Laboratory Procedure

Blood was drawn after an overnight fast, during morning hours in sitting position.

Investigations

1. Serum Lipid Profile **(12hours fasting sample)**

2. Renal parameters (Blood urea, Serum creatinine)

3. Urine spot protein creatinine ratio

4. Fasting plasma Glucose.

All specimens were analysed within 4 to 6 hours of collection. Total cholesterol and triglycerides in the plasma were measured enzymaically and then the cholesterol in the supernant is measured after precipitation of APO-

B containing lipoproteins to determine the HDL cholesterol . LDL cholesterol is estimated by using the friedewald formula.

FRIEDEWALD FORMULA appears to be the most practical reliable method for determining LDL cholesterol in clinical practice.

LDL CHOLESTEROL= CHOLESTEROL – HDL-(TRIGLYCERIDE /5)

VLDL is estimated by dividing the plasma triglycerides by 5 reflecting the ratio of cholesterol to triglyceride in VLDL particles. This formula is reasonably accurate if test results are obtained on fasting plasma and if the triglyceride level is less than 350 mg / dl. The accurate determination of LDL-C levels in patients with triglyceride levels greater than this requires application of Ultra centrifugation techniques (Beta Quantification).

Ethical committee approval **:** Obtained

Consent **:** Informed consent was obtained

Financial support **:** Nil

Conflict of interest **:** Nil

RESULTS AND ANALYSIS

RESULTS AND ANALYSIS

A:CHARACTERISTICS OF RENAL TRANSPLANT (STUDY) CASES AND NORMAL HEALTHY CASES

Table 1 Age

Age	Study Cases		Controls	
	No	**%**	**No**	**%**
< 40	29	72.5	30	75
> 40	11	27.5	10	25
Total	40	100	40	100
Range	26 – 46		25 – 46	
Median	36		34	
Mean	36.4		34.7	
S.D	5.9		6.5	
P	0.1898 (Not Significant)			

There is no statistically significant difference in the age composition of the study and control cases.

Table 2 Sex

Sex	Study Cases		Controls	
	No	**%**	**No**	**%**
Male	33	82.5	30	75
Female	7	17.5	10	25

p = 0.5846 (Not Significant)

The sex composition of the two groups does not have significant difference.

Table 3 BMI

BMI	Study Cases		Controls	
	No	%	No	%
Normal (< 25)	29	72.5	30	75
Cases (> 25)	11	27.5	10	25
Range	18.4 – 28.6		19.4 – 27.0	
Median	23.2		23.1	
Mean	23.1		23.4	
S.D	2.5		2.0	
P	0.5799 (Not Significant)			

The BMI of the two groups does not difference significantly.

Table 4 Free Cholesterol

Free Cholesterol	Study Cases		Controls	
	No	%	No	%
Normal (150-200 mg)	27	67.5	35	87.5
Above normal (>200 mg)	13	32.5	5	12.5
Range	150 – 250		140 – 260	
Median	180		170	
Mean	194.5		179.1	
S.D	36.1		27.6	
p	0.0663			

The mean values of free cholesterol in the study group is higher than that of the control group. But the difference is statistically not significant.

Table 5 TGL

TGL	Study Cases		Controls	
	No	**%**	**No**	**%**
Normal (75-150 mg)	35	87.5	37	92.5
Above Normal (> 150)	5	12.5	3	7.5
Range	100 – 180		90 – 120	
Median	135		120	
Mean	135.5		124.5	
S.D	23.7		28.9	
P	0.0142			

There exists statistically significant difference in the TGL values in the two groups.

Table 6 VLDL

VLDL	Study Cases		Controls	
	No	**%**	**No**	**%**
Normal (20-40 mg)	40	100	39	97.5
Above Normal (> 40)	-	-	1	2.5
Range	20 – 36		18 – 42	
Median	27		24	
Mean	27.1		25.0	
S.D	4.8		5.8	
p	0.0236			

The difference in the VLDL values of the two groups is statistically significant.

Table 7 HDL

HDL	Study Cases		Controls	
	No	**%**	**No**	**%**
Normal (30-60 mg)	40	100	40	100
Below normal (30)	-	-	-	-
Range	30 – 60		40 – 60	
Median	50		50	
Mean	48		52	
S.D	8.0		7.4	
p	0.012			

The difference in the HDL values of the two groups is statistically significant.

Table 8 LDL

LDL	Study Cases		Controls	
	No	**%**	**No**	**%**
Normal (80-150 mg)	32	80	39	97.5
Above normal (> 150 mg)	8	20	1	2.5
Range	80 – 200		70 – 168	
Median	120		96	
mean	121.7		102.2	
S.D	33.3		22.3	
p	0.0222			

The difference in the LDL values of the two groups is statistically significant.

Table 9 Free Cholesterol

	Free Cholesterol				
	Range	**Median**	**Mean**	**S.D**	**P**
Age					
<40 (29)	150 – 270	180	192.8	34.8	0.6798 (Not
> 40 (11)	150 – 280	190	199.1	40.6	Significant)
Sex					
Male (33)	150 – 280	190	199.4	36.1	**0.0271**
Female (7)	150 – 230	160	171.4	27.9	(Significant)
BMI					
Normal (29)	150 – 240	180	183.1	27.3	**0.0027**
Obese (11)	150 – 280	240	224.5	40.3	(Significant)
Follow up					
< 12 months	150 – 280	230	216	41.9	**0.0121**
> 12 months	150 – 240	180	181.6	25.1	(Significant)
Regimen					
2 Drugs	150 – 240	180	181.6	25.1	**0.0121**
3 Drugs	150 – 280	230	216	41.9	(Significant)

Free cholesterol values have statistically significant relationship with Sex, BMI, follow up period and drug regimen of the patient. Their relationship is not significant with age.

Table 10 TGL

	TGL				
	Range	**Median**	**Mean**	**S.D**	**P**
Age					
<40	100 – 180	130	132.4	25.6	0.1274 (Not
> 40	120 – 180	150	143.6	16.3	Significant)
Sex					
Male	100 – 180	140	135.2	22.8	0.8 (Not
Female	110 – 180	120	137.1	29.8	Significant)
BMI					
Normal	100 – 180	130	130.7	2.7	**0.0185**
Obese	100 – 180	150	148.2	22.7	(Significant)
Follow up					
< 12 months	120 – 180	150	150	21.7	**0.0038**
> 12 months	100 – 170	130	126.8	20.8	(Significant)
Regimen					
2 Drugs	100 – 170	130	126.8	20.8	**0.0038**
3 Drugs	120 – 180	150	150	21.7	(Significant)

TGL values have statistically significant relationship with BMI, follow up period and drug regimen of the patients, Age and Sex have no significant relationship will TGL value of renal transplant patients.

Table 11 VLDL

	VLDL				
	Range	**Median**	**Mean**	**S.D**	**P**
Age					
<40	20 – 36	26	26.4	5.2	0.1239
> 40	24 – 36	30	28.7	3.3	(Not significant)
Sex					
Male	20 – 36	28	27.0	4.6	0.1448
Female	22 – 36	24	27.1	6.2	(Not significant)
BMI					
Normal	20 – 36	26	26.1	4.6	**0.0178**
Obese	20 – 36	30	29.6	4.5	(Significant)
Follow up					
< 12 months	24 – 26	30	30	4.3	**0.0035**
> 12 months	20 – 34	26	25.3	4.2	(Significant)
Regimen					
2 Drugs	20 – 34	26	25.3	4.2	**0.003**
3 Drugs	24 – 36	30	30.0	4.3	(Significant)

VLDL values have statistically significant relationship with BMI, follow up period and drug regimen of the patients, Age and Sex have no significant relationship will VLDL value of renal transplant patients.

Table 12 HDL

	HDL				
	Range	**Median**	**Mean**	**S.D**	**P**
Age					
<40	30 – 60	50	48.8	8.0	0.2085
> 40	40 - 60	40	45.9	8.0	(Not Significant)
Sex					
Male	35 – 60	50	48.8	7.9	0.2923
Female	30 – 50	50	44.3	7.9	(Not significant)
BMI					
Normal	35 – 60	50	47.9	7.4	0.8258
Obese	30 – 60	50	48.2	9.8	(Not significant)
Follow up					
< 12 months	40 – 60	50	49.7	8.1	0.3385
> 12 months	30 – 60	50	47.0	7.9	(Not significant)
Regimen					
2 Drugs	30 – 60	50	47.0	7.9	0.3385
3 Drugs	40 – 60	50	49.7	8.1	(Not significant)

HDL values are not significantly affected by age, sex, BMI, follow up period or regimen of drugs.

Table 13 LDL (Taking 150 as cut off value)

	LDL				
	Range	**Median**	**Mean**	**S.D**	**p**
Age					
<40 (29)	80 – 200	96	117.1	32.3	0.1228
> 40 (11)	87 – 180	126	133.7	34.5	(Not significant)
Sex					
Male (33)	80 – 200	120	123.3	33.3	0.3731
Female (7)	86 – 174	94	114.0	34.9	(Not significant)
BMI					
Normal (29)	80 – 170	94	108.8	26	**0.0002**
Obese (11)	120 – 200	160	155.8	25.8	(Significant)
Follow up					
< 12 mo(15)	91 – 200	160	142.3	38	**0.0017**
> 12 mo(25)	80 – 150	95	109.3	23.2	(Significant)
Regimen					
2 Drugs(25)	80 – 150	95	109.3	23.2	**0.0017**
3 Drugs(15)	91 – 200	160	142.3	38	(Significant)

LDL values have statistically significant relationship with BMI, follow up period and drug regimen of the patients, Age and Sex have no significant relationship will LDL value of renal transplant patients.

Table 14 : Relationship of various variables with LDL in study group taking 100 as cut off value for LDL

	LDL			
	Normal		**Abnormal**	
	No	**%**	**No**	**%**
Age				
<40 (29)	15	51.7	14	48.3
> 40 (11)	3	27.3	8	72.7
P	0.1511 (Not significant)			
Sex				
Male (33)	14	42.4	19	57.6
Female (7)	4	57.1	3	42.9
P	0.3825 (Not significant)			
BMI				
Normal (29)	**18**	**62.1**	**11**	**37.9**
Obese (11)	**-**	**-**	**11**	**100**
P	**0.0003 (Significant)**			
Follow up				
< 12 months(15)	5	33.3	10	66.7
> 12 months(25)	13	52	12	48
P	0.4119 (Not significant)			
Regimen				
2 Drugs(25)	13	52	12	48
3 Drugs(15)	5	33.3	10	66.7
P	0.4119 (Not significant)			

When the cut off value for LDL is taken as 100, it brings out statistically significant difference in **BMI.**

Table 15 LDL (Taking 150 as cut off value) and other lipids

	LDL				'p'
	Normal		Abnormal		
	No	%	No	%	
F.C					
Normal	26	96.3	1	3.7	**0.0009**
Abnormal	6	46.2	7	53.8	(Significant)
TGL					
Normal	29	82.9	6	17.1	0.2568
Abnormal	3	60.0	2	40.0	(Not significant)
VLDL					
Normal	32	80	8	20	-
Abnormal	2	-	-	-	
HDL					-
Normal	32	80	8	20	
Abnormal	-	-	-	-	

Table 16 LDL (Taking 100 as cut off value) and other lipids

	LDL				
	Normal		Abnormal		
	No	%	No	%	'p'
F.C					
Normal	18	66.7	9	33.3	**0.0003**
Abnormal	-	-	13	100	(Significant)
TGL					
Normal	18	51.4	17	48.6	**0.04**
Abnormal	-	-	5	100	(Significant)
VLDL					
Normal	18	45.0	22	55	-
Abnormal	-	-	-	-	-
HDL					
Normal	18	45.0	22	55	-
Abnormal	-	-	-	-	-

From Table 15 and Table 16, it is been that when 150 is taken as cut off level, significant abnormalities are observed only in free cholesterol, But when 100 is taken as cut off level for LDL, significant abnormalities are observed both in free cholesterol and TGL levels.

DISCUSSION

DISCUSSION

40 Kidney transplant patients attending the transplant OP, Nephrology Department were taken for the study. Among the 40 patients **33 were males** and **7 were females**. This study was undertaken between the period of 1.8.2005 to 31.5.2006. Informed consent was obtained from all the patients before inclusion in this study. Apart from relevant medical history and physical examination including vitals, Anthropometry & Search for evidence of active infections and Graft rejection done.

A detailed history was taken with emphasis on socioeconomic status and dietary habits. Special consideration was given to findout prior diabetes mellitus (Type 1 or Type2), family history of premature CAD (male before the age of 55 years and females before the age of 65 years) and most probable cause of kidney failure.

Details regarding mode of renal replacement therapy given and, nature of donor and compatibility postoperative complications including graft rejection episodes were recorded well. **Current medical complications** of the patients including hypertension, post transplant diabetes mellitus, (New onset diabetes mellitus), amount of weight gain, possible intercurrent infections were addressed.

Biochemical investigations like **Renal Parameters, Urine Spot PCR, Fasting Lipid profile (12 hours fasting) and Plasma glucose** were done for all of them.40 healthy volunteers attending medical OPD for minor ailments were taken as a control population. Biochemical investigations done after **12 hours of overnight fasting.** All specimens were analysed within 4 to 6 hours of collection. Laboratory procedure for lipid profile analysis included enzymatic method as well as estimation of LDL cholesterol by means of Friedewald formula. Apart from this, Fasting plasma glucose, Blood urea, Serum creatinine and Urine Spot protein creatinine ratio were done for all the patients.

Patients who were known Diabetes Mellitus, Nephrotic syndrome, Hypothyroidism, Liver disease, Clinical and/or Laboratory evidence of renal disease, active intercurrent infections, evidence of graft rejections and substance abuse (Smoking & Alcoholism) were excluded from the study.

Comparative Analysis

In our study 40 patients including 33 males & 7 females were included. Lt Col KV Baliga et al study 15 patients including 12 males & 3 females were participated.

Majority of the patients in our study were in the age group of 26-46 yrs. In KV. Baliga et al study it was between 26-44 yrs.

Most of our patients were males 82.5% (33) and remaining 17.5%(7) were females. In KV. Baliga et al males account for 80% (12) and females for remaining 20% (3).

In our study mean BMI was 23.1 ± 2.5, whereas KV.Baliga et al study it was 21.4± 1.1. So **our study population were slightly heavier than KV. Baliga study population.**

In our study mean free cholesterol levels for patients with transplant duration of < 1yr and > 1yr were found to be 216 & 181mgr%. Corresponding figures in KV. Baliga study were 247 & 212mgr%. So our population had slightly **lower values of free cholesterol irrespective of duration of transplant**. In our study obese patients had mean free cholesterol of 225mgr% & non obese had 183mgr%. This is statistically significant also mean free cholesterol levels for male and female in our study were 199 & 171mgr% respectively. In KV. Baliga et al study these were 232 & 228mgr%. So our population had lower levels of free cholesterol compared to KV. Baliga et al study group.

In our study mean TGL levels for patients with transplant duration of < 1yr and > 1yr were found to be 150 & 126 mgr%. Corresponding figures in KV. Baliga study were 173 & 139mgr%. So our population **had slightly lower values of TGL irrespective of duration of transplant.** In our study obese patients were found to be have higher TGL levels (148mgr %)

compared to non obese patients (130mgr %). This one is statistically significant also. Mean TGL levels for male and female in our study were 135 and 137mgr% respectively. In KV. Baliga et al study these were 158 and 154mgr%. So our population had lower levels of TGL compared to KV. Baliga et al study group.

In our study mean VLDL levels for patients with transplant duration of < 1year and > 1year were found to be 30 & 25mgr% obese patients had mean VLDL of 30mgr% and non obese patients had VLDL 26mgr%. This is statistically significant also. **Mean VLDL levels (27mgr%) for male and female in our study were similar.**

In our study mean HDL levels for patients with transplant duration of < 1year and > 1year were found to be 50 & 47mgr%. Corresponding figures in KV. Baliga study were 45 & 53mgr%. In our study both obese patients and non obese patients had similar HDL levels (48mgr %). Mean HDL levels for male and female in our study were 49 & 44mgr% respectively. In KV. Baliga et al study these were 48 & 52mgr%. So our population had **lower levels of HDL** compared to KV. Baliga et al study group.

In our study mean LDL levels for patients with transplant duration of < 1yr and > 1yr were found to be 142 & 109 mgr%. Corresponding figures in KV. Baliga study were 148 & 118 mgr%. So our population had slightly **lower values of LDL irrespective of duration of transplant**. In our study

obese patients had mean LDL of 155 mgr% & non obese had 108 mgr%. So **obese patients had very high LDL level compared to non – obese patients.** This is statistically significant also. Mean LDL levels for male and female in our study were 123 & 114 mgr% respectively. Male patients had higher LDL level. In KV. Baliga et al study these were 139 & 130 mgr%. So our population had lower levels of LDL compared to KV. Baliga et al study group.

When applied the **NKF recommendations** for the LDL levels of < 100 mg % as a therapeutic goal to our population, only 45% (18) of them were achieved goal LDL. Remaining **55% (22) had high LDL level of more than 100 mg%.**

Among the patients with abnormal LDL levels, most of them were found to be male (19) and remaining were females (3) in absolute numbers. Out of 33 male patients 24 were below the age of 40 years and remaining 9 were above the age of 40 years. Out of 33 male patients 19 had abnormal LDL level (58%). Among the 19 male patients 12 were below the age of 40 years (63%). Remaining 7 were above the age of 40 years (78%).

Out of 7 females 5 were below the age of 40 and 2 were above the age of 40. Out of 3 females one is below the age of 40 years (20%). Remaining 2 were above the age of 40 years (100%).

So, **abnormal LDL levels were seen more among above the age of 40 years group.**

SUMMARY

SUMMARY

1. Most of the kidney transplant patients are **below the age of 40 years**. Age group ranges from 26 – 46 years. 29 out of 40 are below 40 years (72.5%).

2. **Male predominance** is seen among the kidney transplant population. 33 out of 40 (82.5%) of them are male. Most of the male patients had lipid profile abnormalities.

3. Majority of the kidney transplant patients are **non-obese** as evidenced by BMI of less than 25. 29 out of 40 patients (72.5%) had BMI of less than 25. Remaining 27.5% are obese with BMI of more than 25. Most of the obese patients had abnormal lipid profile.

4. 15 out of 40 patients are on **triple drug regimen (Prednisolone, Azathioprine & Cyclosporine**). Remaining 25 are on double drug regimen (Prednisolone, Azathioprine).

5. Total cholesterol levels are within normal limits for 27 patients (67.5%). Remaining 13 **(32.5%) had elevated total cholesterol.**

6. 35 out of 40 patients (87.5%) had normal triglyceride levels. Remaining 5 patients (12.5%) had elevated triglyceride levels.

7. VLDL levels are normal for all 40 patients (100%).

8. All patients had **normal HDL cholesterol levels** (100%).

9. LDL cholesterol levels are normal for 32 patients (80%) if LDL cut off of more than 150 mg / dl is taken. If more than 100 mg / dl is taken as abnormal **(NKF recommendation)** then 22 patients **(55 %)** were not on the goal LDL level.

10. Majority of patients on triple drug regimen were found to be having abnormal total cholesterol, triglyceride, VLDL, HDL and LDL.

11. Majority of the patients **above the age of 40 years** had abnormal LDL levels **irrespective of gender.**

12. Those on **triple drug regimen** (Prednisolone, Azathioprine & Cyclosporine) were found to be having **abnormal levels of LDL**.

CONCLUSION

CONCLUSION

In our population, on applying **NKF recommendations**

1. **55% of the patients had abnormal LDL levels.**
2. 58% of the males and 42% of females were found to be have abnormal LDL levels.
3. Below the age of 40 years, 50% of the males and 20% of the females had abnormal LDL levels.
4. **Majority of the patients above the age of 40 years had abnormal LDL levels.(78% of the males and 100% of females).**
5. Majority of the patients on **triple drug regimen (Prednsiolone, Azathioprine & Cylcosporine)** were found to be have abnormal LDL levels.

In order to achieve therapeutic LDL level of < 100 mg% in our population, **Therapeutic lifestyle change (TLC)** should be the first measure. Even after 3 months of adequate therapeutic lifestyle change **(TLC),** if LDL goals are not achieved **statins** should be started. Lowest effective dose of statin should be started and titrated accordingly. Frequent monitoring of liver function tests and creatinine phospho kinase is needed.

APPENDIX

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BIBLIOGRAPHY

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PROFORMA

PROFORMA

Name : Age :

Sex : Occupation :

Address :

History

1. Probable cause of renal failure
2. Mode of renal replacement therapy given prior to transplant – HD / PD
3. Nature of Donor – (Related / Unrelated / Cadaveric) & compatibility
4. Post operative complications - including rejection
5. Immunosuppressive drug regimen and amount of weight gain
6. Prior Comorbid medical illness

Clinical Examination

1. Vital parameters
2. Height, Weight, Body Mass Index
3. Major systems examination
4. Evidence of Active infections / graft rejection

Biochemical Investigations

1. 12 hours Fasting Lipid Profile
    - ★ Free cholesterol
    - ★ Triglycerides
    - ★ HDL, LDL, VLDL
2. Renal parameters (Blood Urea, Serum Creatinine)
3. Fasting Plasma Glucose
5. Urine spot protein creatinine ratio

MASTER CHART

MASTER CHART

S.No	GROUP	AGE (years)	Ht. (cm)	BMI	Wt(Kg)	FOLLOW UP	REGIMEN	Sex	FC (mg%)	TG (mg%)	HDL (mg%)	LDL (mg%)	VLDL (mg%)
1	STUDY	27	156	23.8	58	15	2	1	180	100	35	125	20
2	STUDY	34	160	22.7	58	15	2	1	160	100	50	90	20
3	STUDY	38	160	23.4	60	18	2	1	150	100	45	85	20
4	STUDY	29	154	27.0	64	8	3	1	240	180	40	164	36
5	STUDY	31	158	24.0	60	18	2	1	160	110	45	93	22
6	STUDY	34	160	19.5	50	16	2	1	170	150	45	95	30
7	STUDY	36	156	23.8	58	10	3	1	230	180	50	144	36
8	STUDY	34	156	22.2	54	14	2	1	190	130	40	124	26
9	STUDY	40	158	24.0	60	8	3	1	230	150	40	160	30
10	STUDY	34	154	22.8	54	16	2	1	160	100	50	90	20
11	STUDY	26	156	25.5	62	14	2	1	190	100	50	120	20
12	STUDY	28	158	25.6	64	6	3	1	280	150	50	200	30
13	STUDY	33	154	26.1	62	8	3	1	250	150	50	170	30
14	STUDY	36	160	21.9	56	18	2	2	150	110	40	88	22
15	STUDY	28	154	21.9	52	18	2	2	160	120	50	86	24
16	STUDY	32	156	22.2	54	10	3	2	230	180	50	144	36
17	STUDY	38	152	26.0	60	14	2	2	180	120	30	126	24
18	STUDY	42	156	25.5	62	9	3	2	150	180	40	174	36
19	STUDY	40	156	20.5	50	15	2	2	160	120	50	86	22
20	STUDY	46	158	18.4	46	10	3	2	170	130	50	94	26
21	STUDY	33	156	21.4	52	11	3	1	180	120	60	96	24
22	STUDY	29	158	19.2	48	10	3	1	180	120	55	91	24
23	STUDY	32	160	23.4	60	14	2	1	230	170	50	146	34
24	STUDY	42	158	19.2	48	7	3	1	160	130	40	94	26
25	STUDY	44	156	20.5	50	17	2	1	160	140	45	87	28
26	STUDY	35	150	25.8	58	14	2	1	240	150	60	150	30
27	STUDY	39	160	19.5	50	15	2	1	180	130	60	94	26
28	STUDY	31	156	23.0	56	14	2	1	220	150	50	140	30
29	STUDY	40	160	24.2	62	15	2	1	200	140	40	132	28
30	STUDY	41	164	23.8	64	8	3	1	240	150	40	170	30
31	STUDY	46	158	25.6	64	15	2	1	200	150	50	120	30

S.No	GROUP	AGE (years)	Ht. (cm)	BMI	Wt(Kg)	FOLLOW UP	REGIMEN	Sex	FC (mg%)	TG (mg%)	HDL (mg%)	LDL (mg%)	VLDL (mg%)
32	STUDY	44	152	28.6	66	14	2	1	220	150	40	150	30
33	STUDY	37	164	21.6	58	15	2	1	170	140	50	92	28
34	STUDY	44	150	26.7	60	8	3	1	250	150	60	160	30
35	STUDY	29	164	21.6	58	18	2	1	180	140	60	92	28
36	STUDY	45	156	25.5	62	8	3	1	270	150	60	180	30
37	STUDY	33	180	18.5	60	8	3	1	180	130	60	94	26
38	STUDY	45	160	22.7	58	14	2	1	190	130	40	126	26
39	STUDY	44	150	24.9	56	16	2	1	180	120	40	116	24
40	STUDY	36	170	20.1	58	18	2	1	160	100	60	80	20
41	CONTROL	29	156	23.8	58			1	170	130	50	94	26
42	CONTROL	32	160	21.9	56			1	180	120	60	96	24
43	CONTROL	34	158	21.6	54			1	140	90	40	82	18
44	CONTROL	34	160	21.1	54			1	150	100	50	80	20
45	CONTROL	30	152	24.2	56			1	160	100	50	90	20
46	CONTROL	28	156	23.0	56			1	190	150	60	100	30
47	CONTROL	44	156	23.8	58			1	200	140	50	122	28
48	CONTROL	40	158	24.0	60			1	260	210	50	168	42
49	CONTROL	26	156	26.3	64			1	180	100	60	100	20
50	CONTROL	42	152	26.0	60			1	195	120	40	131	24
51	CONTROL	46	158	24.8	62			1	200	150	40	130	30
52	CONTROL	43	154	26.1	62			1	160	100	40	100	20
53	CONTROL	28	156	23.8	58			1	170	120	60	86	24
54	CONTROL	34	154	21.1	50			1	180	120	60	96	24
55	CONTROL	38	156	22.2	54			1	180	150	40	110	30
56	CONTROL	28	160	22.7	58			1	190	150	60	100	30
57	CONTROL	42	150	22.2	50			1	190	140	40	122	28
58	CONTROL	27	160	21.1	54			1	180	130	60	94	30
59	CONTROL	34	158	25.6	64			1	170	120	50	96	24
60	CONTROL	36	156	21.4	52			1	160	120	50	84	24
61	CONTROL	28	160	25.8	66			2	170	110	60	88	22
62	CONTROL	31	156	22.2	54			2	170	120	50	96	24
63	CONTROL	39	172	20.3	60			2	160	110	60	78	22
64	CONTROL	36	170	19.4	56			2	150	100	50	80	20

S.No	GROUP	AGE (years)	Ht. (cm)	BMI	Wt(Kg)	FOLLOW UP	REGIMEN	Sex	FC (mg%)	TG (mg%)	HDL (mg%)	LDL (mg%)	VLDL (mg%)
65	CONTROL	45	156	26.3	64			2	240	200	50	150	40
66	CONTROL	37	168	21.3	60			2	150	100	40	90	20
67	CONTROL	35	170	20.8	60			2	160	100	50	90	20
68	CONTROL	43	154	26.1	62			2	250	200	60	150	40
69	CONTROL	33	160	22.7	58			2	170	100	50	100	20
70	CONTROL	45	158	24.8	62			2	180	110	60	98	22
71	CONTROL	32	154	27.0	64			1	160	100	50	110	20
72	CONTROL	27	152	26.0	60			1	170	100	50	100	20
73	CONTROL	25	164	20.8	56			1	150	100	60	70	20
74	CONTROL	44	150	23.1	52			1	220	150	60	130	30
75	CONTROL	26	162	22.1	58			1	160	100	60	80	20
76	CONTROL	44	164	22.3	60			1	170	110	60	88	22
77	CONTROL	27	156	24.7	60			1	230	150	60	140	30
78	CONTROL	31	162	22.1	58			1	170	120	50	96	24
79	CONTROL	34	160	24.2	62			1	170	120	60	86	24
80	CONTROL	29	158	25.6	64			1	160	120	50	86	24

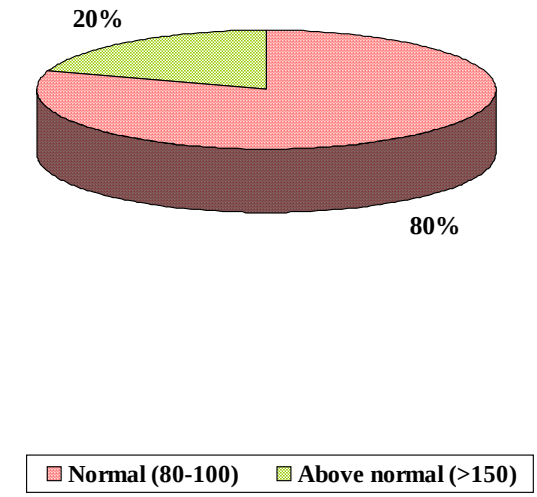
Sex 1 - Male

2 - Female

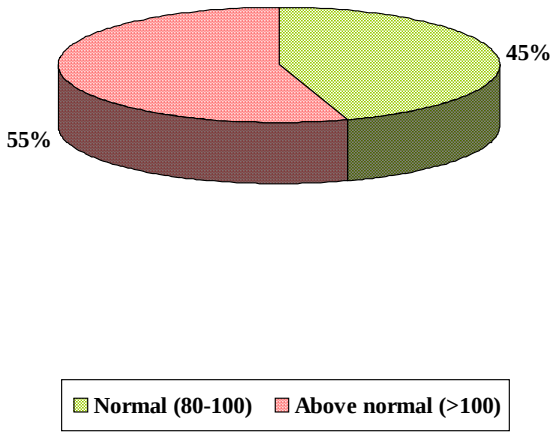
Regimen 3 - Triple Drug

2 - Double drug

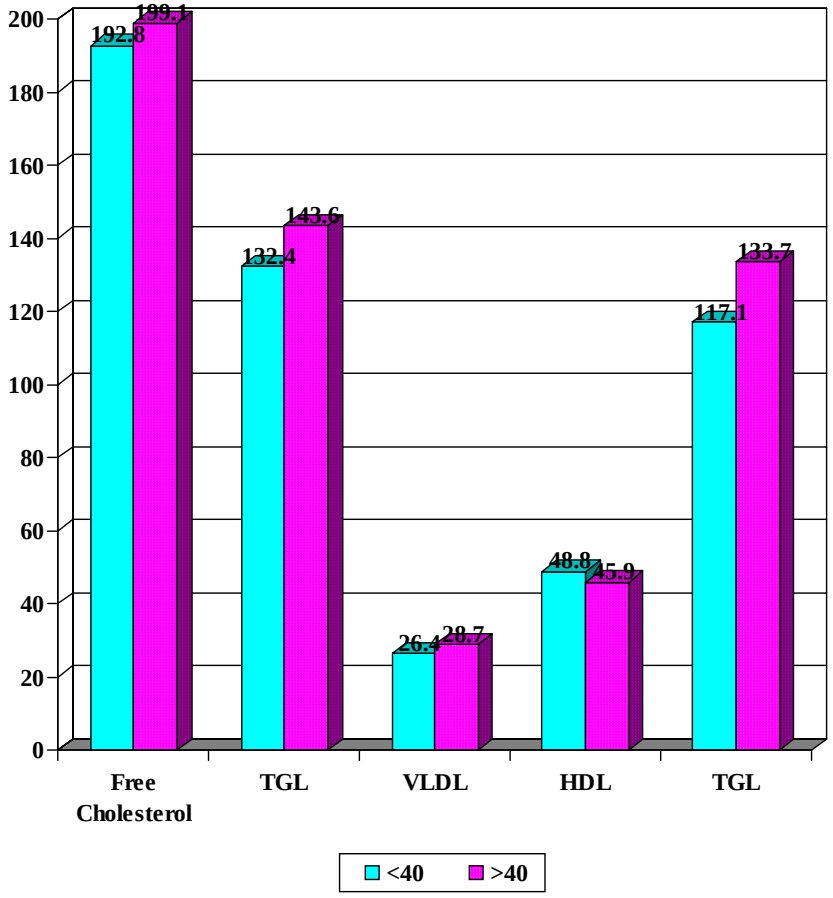
LDL (cut off 150)



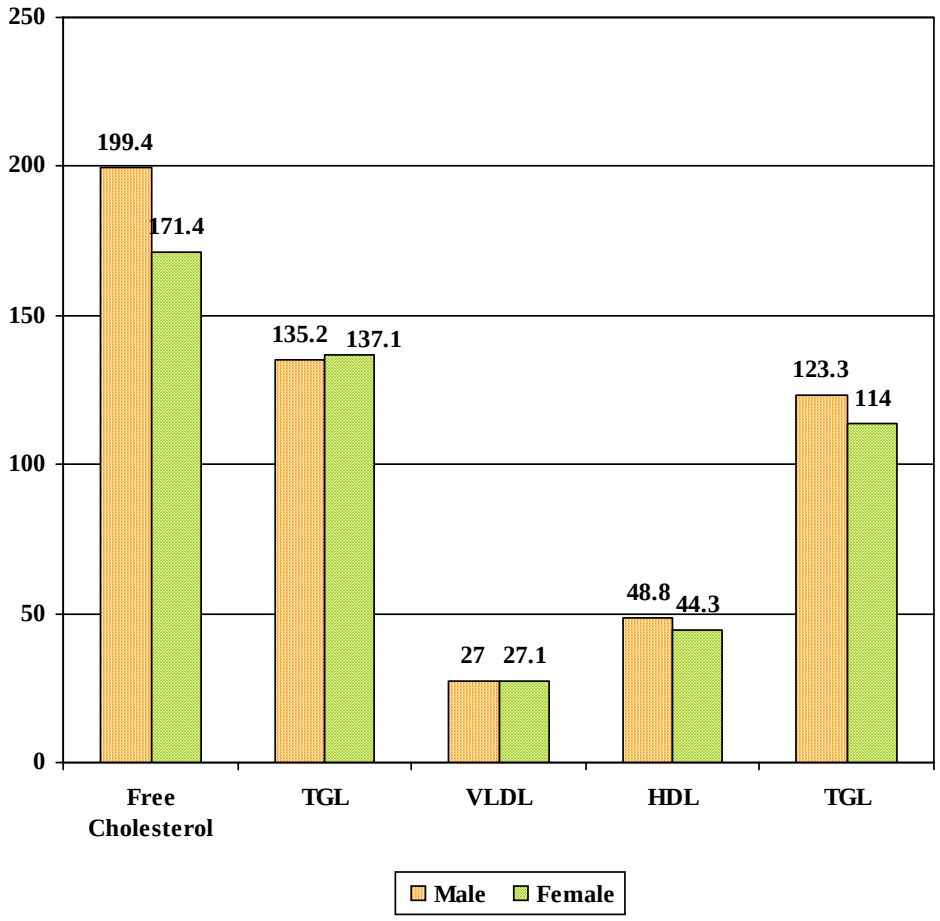
LDL (cut off 100)



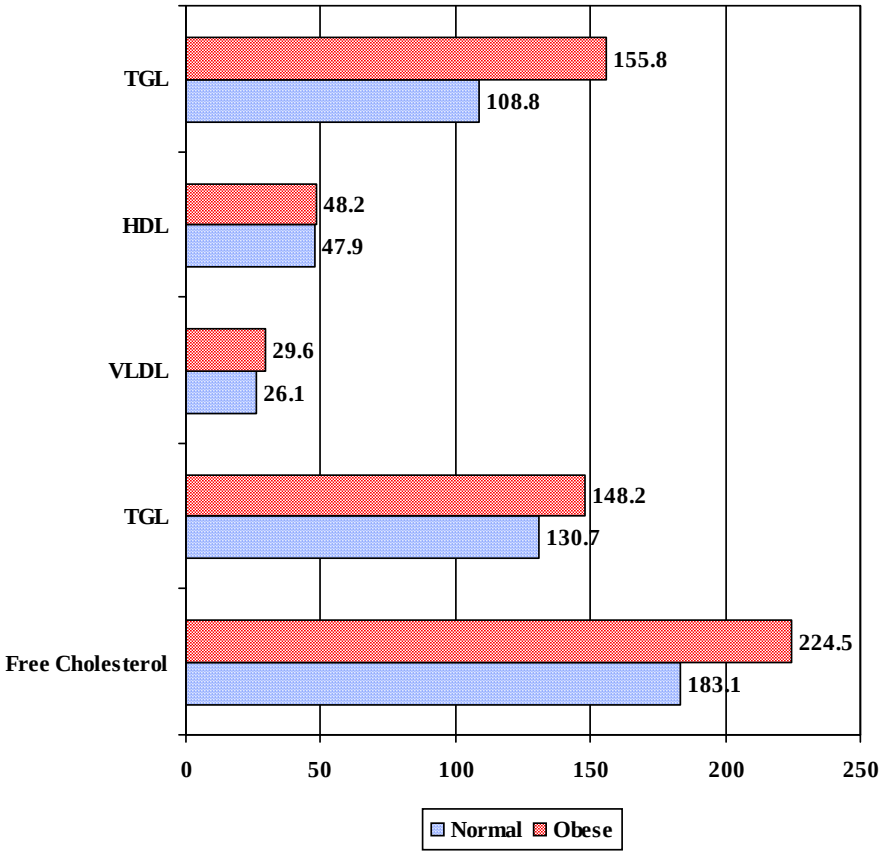
Age


200
180
160
140
120
100
80
60
40
20
0
192.8
199.1
132.4
143.6
26.4
28.7
48.8
45.9
117.1
133.7
Free Cholesterol
TGL
VLDL
HDL
TGL
<40
>40

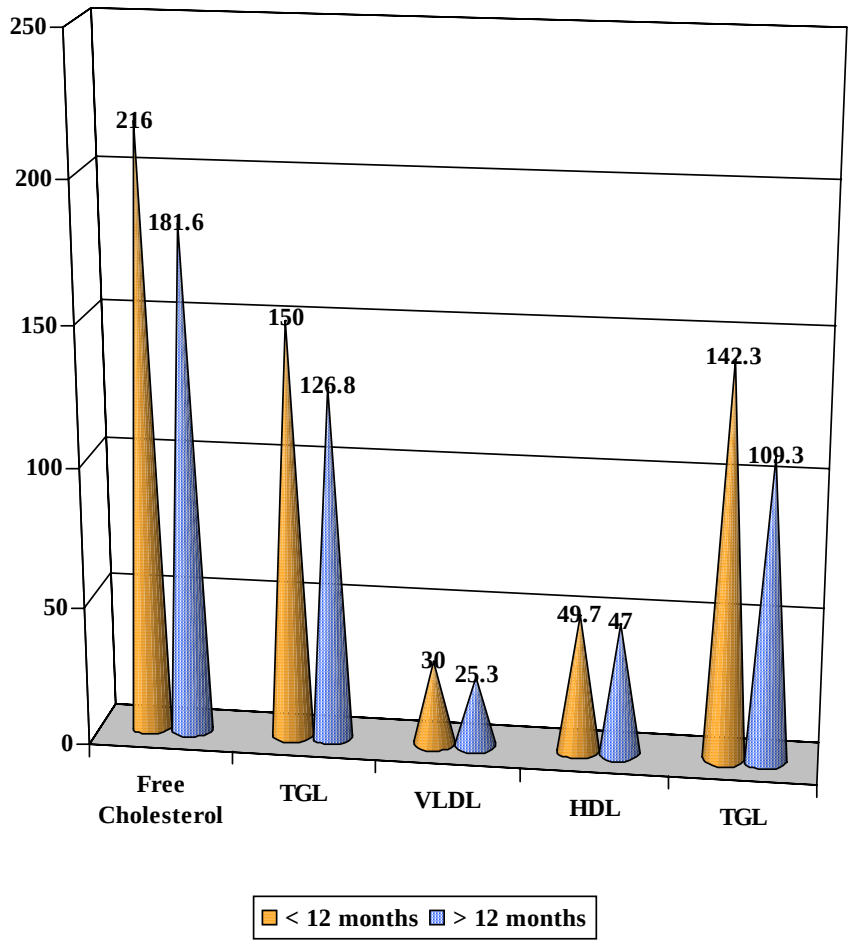
Sex


250
200
150
100
50
0
199.4
171.4
135.2
137.1
27
27.1
48.8
44.3
123.3
114
Free Cholesterol
TGL
VLDL
HDL
TGL
Male
Female

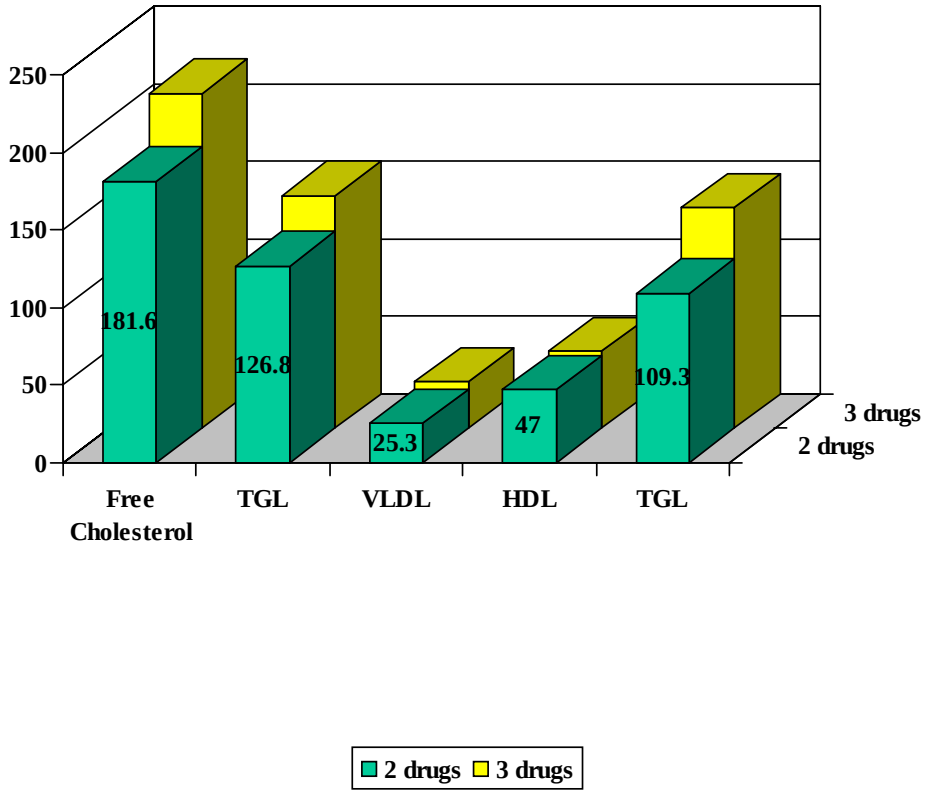
BMI


TGL
155.8
108.8
HDL
48.2
47.9
VLDL
29.6
26.1
TGL
148.2
130.7
Free Cholesterol
224.5
183.1
0
50
100
150
200
250
Normal
Obese

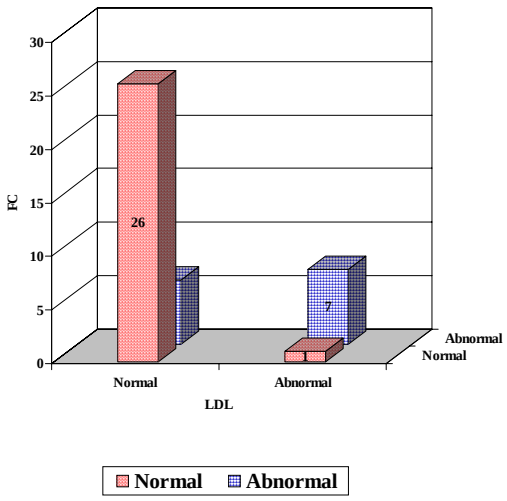
Follow up

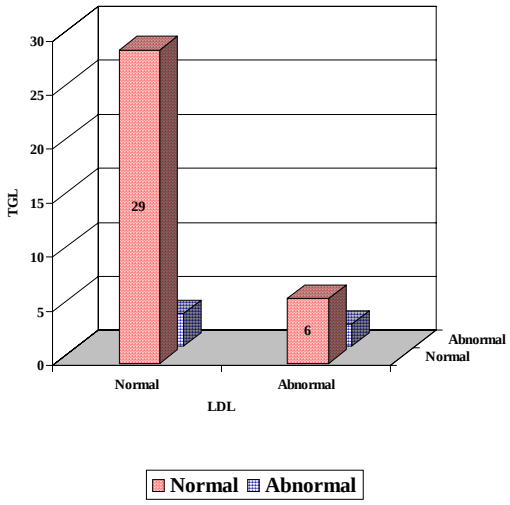

250
200
150
100
50
0
216
181.6
150
126.8
30
25.3
49.7
47
142.3
109.3
Free Cholesterol
TGL
VLDL
HDL
TGL
< 12 months
> 12 months

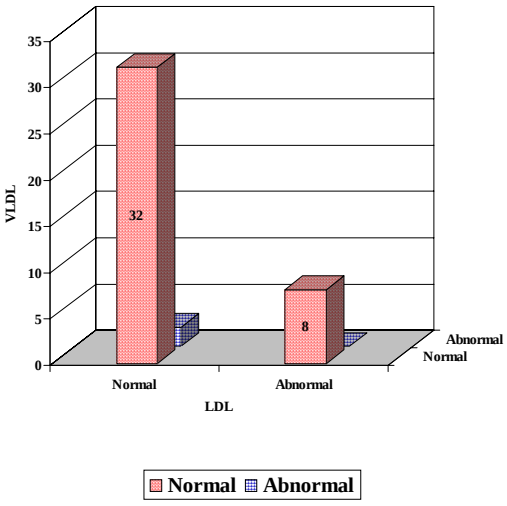
Regimen

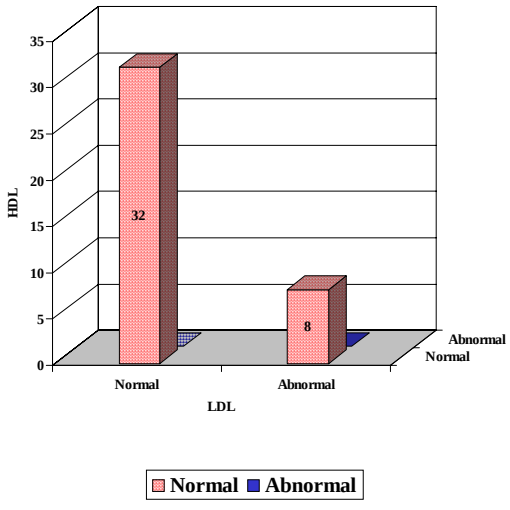

250
200
150
100
50
0
181.6
126.8
25.3
47
109.3
3 drugs
2 drugs
Free Cholesterol
TGL
VLDL
HDL
TGL
2 drugs
3 drugs

LDL (Taking 150 as cut off value) and other lipids









LDL (Taking 100 as cut off value) and other lipids